ABSTRACTS OF WORLD MEDICINE

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Hygiene and Public Health

2650. **Poliomyelitis and the Social Environment**
A. B. HILL and W. J. MARTIN. *British Medical Journal* [*Brit. med. J.*] **2**, 357–358, Aug. 13, 1949. 6 refs.

It has been suggested that towns with favourable health conditions as revealed by low infant and general mortality rates are peculiarly liable to a heavy incidence of poliomyelitis when that disease becomes epidemic. The recorded notifications of poliomyelitis in the 273 large and small towns of England and Wales show no such association between the attack rates they suffered in the 1947 epidemic and the infant and general death rate they experienced in the two preceding years, 1945–6. In other words, according to this experience, favourable mortality rates, indicating social conditions in a locality, need not raise fears of an unduly heavy risk when poliomyelitis becomes widespread.—[Authors' summary.]

2651. **Prophylaxis of Exanthematic Typhus in Times of Epidemic and in Interepidemic Periods in Algeria.** (La prophylaxie du typhus exanthématique en temps d'épidémie et dans les périodes interépidémiques en Algérie)
E. SERGENT, M. BÉGUET, L. PARROT, and R. HORRENBERGER. *Archives de l'Institut Pasteur d'Algérie* [*Arch. Inst. Pasteur Algér.*] **27**, 1–6, March, 1949. 3 refs.

Methods of eradicating typhus and their application in Algeria are discussed in this article. The measures employed must take into consideration: (1) that epidemic periods of 3 to 4 years' duration are usually succeeded by relatively silent spells lasting for some 8 to 12 years; and (2) that the greater part of the population is constantly on the move, which renders anti-louse treatment with DDT powder of only transitory value and makes mass immunization by three injections at weekly intervals impossible.

The technique adopted in Algeria since 1943, on the recommendation of the Pasteur Institute of Algeria, is to attack the disease in two ways: (1) In an epidemic, by isolation of typhus patients and of direct contacts, and by disinfestation of all other local inhabitants with DDT and their inoculation (for which the killed vaccine of Durand and Giroud, produced at the institute, is used). (2) In endemic areas, by the immunization of the entire population with a single 2 ml. dose of vaccine at yearly intervals, instead of the normal course of three inoculations of 1 ml. each at weekly intervals. It is claimed that in populations in which typhus is endemic a satisfactory resistance can be obtained in this way, without untoward reactions. *W. G. Harding*

2652. **The Foley–Parrot Method for Mass Anti-tuberculosis Vaccination in the Tropics by B.C.G.** (La méthode Foley—Parrot pour la vaccination antituberculeuse collective outre mer par le B.C.G.)
E. SERGENT. *Archives de l'Institut Pasteur d'Algérie* [*Arch. Inst. Pasteur Algér.*] **17**, 7–17, March, 1949. 2 figs., 11 refs.

This is a brief description of a method of mass vaccination of native populations with B.C.G., based on the work of Foley and Parrot in Algeria. Owing to the difficulty of assembling the members of nomadic tribes on four separate occasions in order to administer tuberculin, read skin reactions, and immunize those found to be tuberculin-negative, it was decided to undertake the vaccination by cutaneous scarification of all children below 15 and their revaccination every 3 years up to that age. Since 1933 some 20,000 children have been vaccinated and the author claims that no harm results from the immunization of tuberculin-positive subjects by this method. *W. G. Harding*

2653. **Cyanosis of Infants Produced by High Nitrate Concentration in Rural Waters of Saskatchewan**
H. E. ROBERTSON and W. A. RIDDELL. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **40**, 72–77, Feb., 1949. 7 refs.

Almost one-third of water samples from rural wells in Saskatchewan were found to contain more than 10 parts per million (p.p.m.) of nitrate and one-quarter to contain more than 20 p.p.m. Most of the bad samples came from dug wells. In a period of 6 months 10 infants were reported in the Regina area as suffering from cyanosis, the cause of which was established as methaemoglobinaemia. There were two fatal cases, in both of which the water used in preparing the infants' feeds contained more than 1,000 p.p.m. of nitrate.
Scott Thomson

2654. **Studies on Tetanus Immunization in the R.C.A.F.**
J. M. MATHER, A. D. MCCLURE, R. F. FARQUARSON, and A. H. SELLORS. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **40**, 51–59, Feb., 1949. 1 ref.

The concentration of circulating tetanus antitoxin was determined in samples of blood from over 1,000 airmen who had been actively immunized by injection of tetanus toxoid. Over 95% contained more than 0·1 unit of antitoxin per ml. and 99·6% contained 0·01 unit or more.

None of the men whose blood contained less than 0·01 unit had received the full course of injections. Most of the samples were taken within 2 years of the injections. These concentrations of antitoxin found in the actively immunized were greater than those found a few days after the injection of a prophylactic dose of antitoxin. The authors suggest that the administration of tetanus antitoxin at the time of wounding of a properly immunized soldier is unnecessary. *Scott Thomson*

2655. **Bacteria on Bank Notes**
B. R. NISBET and T. SKEOCH. *Medical Officer* [*Med. Offr*] **131**, 225–226, May 28, 1949. 6 refs.

The authors examined 36 bank notes from 4 different sources by rubbing each with a swab moistened in glucose broth, from which tubes of glucose broth and tellurite plates were inoculated and incubated overnight. Subcultures were then made from the broth tubes on to fresh blood agar and gentian violet blood agar plates which were incubated for a further 18 hours. The majority of notes yielded bacteria of non-pathogenic species, but 7 of the 36 were found to be contaminated with pathogenic organisms—3 with *Staphylococcus aureus*, 2 with *Staph. aureus* and *Streptococcus haemolyticus*, 1 with *Pneumococcus* and *Staph. aureus*, and 1 with *Pneumococcus* alone.

The authors conclude that a not inconsiderable risk may be run by those handling large numbers of bank notes and they suggest that those counting paper notes should use a sponge impregnated with some non-irritant disinfectant for moistening the fingers. They further advocate the withdrawal from circulation of all dirty notes [a most timely recommendation, as at present the Treasury urges banks to keep notes in circulation longer than has been customary hitherto]. The authors also suggest the consideration of methods of disinfecting bank notes before re-issue from the bank.

K. Zinnemann

2656. **The Epidemiology of Yellow Fever in Central Africa**
A. F. MAHAFFY. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **42**, 511–524, May, 1949. 2 figs., 27 refs.

The modern conception of the epidemiology of yellow fever in Central Africa is based almost exclusively on investigations carried out in Bwamba County, a small, heavily forested area in the extreme west of Uganda. Work started in 1937 and it was shown that, once yellow fever became established in man, the vector of importance in this area was *Aëdes simpsoni*, a semi-domestic species, but that epidemic outbreaks in the human population were associated with contact with the uninhabited forest, where *A. simpsoni* was not found. *A. aegypti* was present in both inhabited and forest areas, but in small numbers only, and it was established that within the forest the infection is kept alive by a monkey-mosquito cycle, the vector being the highly arboreal *A. africanus*. It appears that man does not readily become infected inside the forest, owing to the low concentration of the vector at ground level: in this, African yellow fever differs from the jungle yellow fever of South America. The greatest incidence of yellow fever in man is found along the forest boundary where the vertebrate hosts, man and monkey, and both sylvan and human vectors are close together. The infection probably reaches man via *A. simpsoni*, which is known to enter the forest edge, to feed on both man and monkeys, and to bite at both ground and higher levels.

[This important paper includes a review of recent articles on the epidemiology of yellow fever in West Africa, and of the stages by which the above conclusions have been reached.] *W. H. Horner Andrews*

INDUSTRIAL MEDICINE

2657. **Sickness Absence due to Peptic Ulcers**
R. DOLL and M. M. BUCKATSZCH. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **6**, 100–102, April, 1949. 4 refs.

The sickness absence of men with peptic ulcers was determined among 2,871 employees of seven firms, six in London and one in a small provincial town, and compared with that of controls of the same age and similarly employed. Of all employees 5·4% had been shown to have a peptic ulcer, and their mean sickness absence was 6 working days a year more than that of controls. Thus it is calculated that 32·4 working days a year per hundred men are lost as a result of peptic ulcer. *C. Bruce Perry*

2658. **Arsine Poisoning as a Result of the Use of Acid for Scaling.** (L'intoxication par l'hydrogène arsénié au cours du détartrage par les acides)
—. ASSOULY and —. GRIFFON. *Archives des Maladies Professionnelles* [*Arch. Mal. prof.*] **10**, 337–346, 1949. 2 figs., 19 refs.

This valuable paper gives a detailed description of the poisoning by arsine of two workers employed in the chemical removal of chalky deposits in a hot-water bath. One man died at the end of a week and the diagnosis of arsenical poisoning was confirmed at necropsy; the other recovered, but only after he had sustained a massive haemolysis, his erythrocyte count being reduced to 1,430,000 per c.mm. and his haemoglobin concentration to 40%, with consequent reddening of the serum, intense jaundice, blackening of the urine, and cyanosis of limbs. Some improvement was noticed on the third day of his illness, when a course of treatment with BAL was started, but regeneration of erythrocytes was slow; on the 14th day they numbered only 2,080,000 per c.mm. Sternal puncture on the 9th day revealed no abnormal elements, but there was a definite erythroblastic reaction with an increase in the number of the myelocytes.

These men had been employed on what seemed a small job of little importance. The water bath was of 120-litre capacity, in a small room of 7 c.m. furnished with one small window, which was shut. They omitted all precautions, did not attach to the upper part of the vessel a system of rubber piping for the escape of any gases formed, allowed no general ventilation, and used a

stronger acid solution than was advisable. Even when gases were being evolved in quantity they remained at their work for a total period of 2½ hours.

A full description is given of the methods employed in the chemical scaling of hot water systems. The solvent generally used is hydrochloric acid, its alkaline earth salts being soluble. This commercial acid contains a small quantity of arsenic as an impurity. To it must be added some other substance to protect from the acid the metal uncovered as the work proceeds. One protective agent is arsenic anhydride, As_2O_3, 3 to 4 g. per litre of the concentrated acid, metallic arsenic being deposited upon the exposed iron. Zinc, galvanized iron, or aluminium, however, are not protected, the acid attacking the metal and releasing arsenic; this reaction is augmented by the presence of arsenic in the solution.

It is urged that workmen so employed should carry respirators fitted with activated charcoal with the addition of a solution of sulphate of copper in glycerin, the only type of filter which protects from arsine. It is recommended that chemical scaling of hot-water systems be added to the statutory list of operations which may be the cause of arsenical poisoning.

M. A. Dobbin Crawford

2659. **Epidemic Kerato-conjunctivitis in Workers in Metallurgical Factories in the Paris Region.** (La kérato-conjonctivite épidémique des ouvriers des usines de métallurgie de la région Parisienne)
A. HADENGUE. *Presse Médicale* [*Pr. méd.*] **57**, 482–483, May 28, 1949. 2 refs.

A sudden outbreak of kerato-conjunctivitis occurred in a large factory in Paris and, by reason of its rapid spread, led to the suspicion that a new disease had appeared. The author points out, however, that such epidemics are well known and are not strictly of occupational origin, though they often arise in industrial groups.

The incubation period is 5 to 8 days. The condition may be noted after efforts to remove a foreign body and at first causes severe lacrimation and swelling of the lids, the lower conjunctival sac being conspicuously more severely involved. An enlarged pre-auricular lymph node, usually present, is considered to be diagnostic. After 2 days a follicular conjunctivitis confined to the lower lid is seen and a little later false membrane may form which detaches easily. This stage lasts for from 1 to 3 weeks. Keratitis is the essential sign of the disorder, usually appearing after the 8th day but perhaps as late as 3 weeks after the onset. It is punctate or nodular-epithelial in type. The centre of the cornea is generally involved and the lesions rarely ulcerate but may last for as long as 2 years. Healing generally occurs with some loss of visual acuity.

Infection appears to be carried by dust, by towels, and by other means of direct spread. In the epidemic described, and in earlier ones, experimental lesions were induced in man and in animals by inoculation with tears. It appears that a virus of the order of 50 mμ. in size is responsible and this is resistant to most of the antiseptics in general use. Infection confers later immunity. Although the disorder is distressing, most of those attacked are able to work. Hygienic measures should include the prohibition of communal use of towels, the use of individual protective spectacles, and special measures for sterilization of all ophthalmic instruments and equipment.

The factory mentioned was engaged in metallurgical work and, though the disease cannot strictly be considered occupational, yet the number of cases detected in the workers' families was small. The disorder should be considered more as an industrial accident than an industrial disease. *G. C. Pether*

2660. **Glass-wool Dermatitis.** (Dermatitis por la "lana de vidrio")
J. M. T. BONA. *Actas Dermo-sifiliográficas* [*Actas Dermo-sif.*] **40**, 629–632, March, 1949.

Contact with glass-wool generally produces an itchy, erythematous, small papular eruption of follicular distribution on the hands, forearms, and neck, seldom on covered parts. Minute fragments of glass fibre can be seen with a magnifying glass. The condition is usually unimportant, but secondary infection and pustulation may occur. A large percentage of workers using glass-wool are affected in varying degrees. In 36 of 42 cases studied by the author pulp infections of the tips of the thumbs and the index and middle fingers were discovered.

James Marshall

2661. **Acute Dermatitis and Pneumonitis in Beryllium Workers: Review of 406 Cases in Eight-year Period with Follow-up on Recoveries**
J. M. DENARDI, H. S. VAN ORDSTRAND, and M. G. CARMODY. *Ohio State Medical Journal* [*Ohio St. med. J.*] **45**, 567–575, June, 1949. 2 figs., 5 refs.

This report deals only with acute manifestations encountered in the three plants of two companies in the Cleveland area. Of the 406 cases, 195 were of cutaneous and 211 of respiratory disease.

The skin lesions are considered to be due to beryllium sulphate tetrahydrate, anhydrous beryllium sulphate, beryllium fluoride, and ammonium beryllium fluoride and their solutions. Beryllium metal alone does not affect the skin. Lesions may result from a combination of individual hypersensitivity with the irritating effects of the acid radical. The symptoms are burning and pruritus. Usually lesions are confined to the exposed parts, but in cases of hypersensitivity there is widespread distribution with urticarial reaction. Of new employees exposed to beryllium salts 25% show allergic reactions on the exposed parts in 3 to 10 days. [The abstracter's experience suggests that this is a low estimate of morbidity.] Urticarial, hyperaemic, discrete papular, papulo-vesicular, and ulcerative lesions are described. After apparent cure relapse occurred in spite of protection in a high percentage of severe cases. Also, numerous persons with dermatitis developed bronchitis and pneumonitis when continuing the same work. Hence severe dermatitis in new workers indicates susceptibility to pulmonary irritation. Treatment consists of the use of antipruritic applications and antihistaminic drugs.

Ulceration is caused by the intrusion of crystals of beryllium fluoride or beryllium sulphate tetrahydrate into an abrasion. Hydrolysis of the crystal releases the acid radical which destroys surrounding tissue. The surface layer heals over the ulcer, forming a papule and later an abscess. The papule should be incised, any crystals removed, and the fibrous base curetted. Healing is by second intention in 7 to 14 days.

Pneumonitis is of two types, fulminating and insidious. The former is less common and due to brief exposure to high concentrations of anhydrous beryllium sulphate fumes derived from the interaction of finely pulverized beryllium ore frit with sulphuric acid. Within 72 hours of exposure spasmodic cough, tightness of the chest and substernal pain, severe exertional dyspnoea, and varying degrees of cyanosis appear. Examination reveals acrocyanosis, sudden decrease in vital capacity, limited chest expansion, and sibilant rales throughout. Recovery takes place in 7 to 16 days. The insidious variety usually follows exposure to fumes or dusts of beryllium sulphate tetrahydrate, beryllium fluoride, or beryllium oxide. Symptoms consist of dyspnoea on slight exertion, spasmodic cough, sputum rarely blood-streaked, substernal burning pressure or pain, tightness of chest especially on inspiratory effort, general weakness, anorexia, and loss of weight. There are a pronounced fall in vital capacity, acrocyanosis, fine to coarse inspiratory rales, and sibilant rhonchi, at first over the bases and later the hila, with increased pulse and respiratory rates and a normal temperature. Recovery takes place in 4 to 12 weeks. Radiological changes do not usually appear until 1 to 3 weeks after the onset of symptoms in both types of the disease. There is then ". . . a particular type of peribronchial haziness and punctate infiltration usually scattered throughout the lower half of each lung field which gives the almost granular appearance seen in pneumoconiosis or one of the mycotic lesions. In severe cases this punctate infiltration progresses to actual consolidation with the " snow flurry " effect resembling at times malignant metastatic lesions ". Treatment of both types consists in administration of oxygen, penicillin, and antihistaminic drugs.

Twenty illustrative cases are described. [In case 17 the diagnosis is suggested by the clinical findings, but the industrial history (stenographer) might have been amplified. In the film described as negative (Figure 2) there are discrete nodular shadows, but these are possibly artefacts.] *H. Wyers*

2662. **Manganese Pneumonitis. Further Clinical and Experimental Observations**
T. A. Lloyd Davies and H. E. Harding. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **6**, 82–90, April, 1949. 13 figs., 10 refs.

In the years 1938–47 the incidence of " pneumonia " in employees in a manganese plant who were exposed to inhalation of manganese oxide and higher oxides of manganese was very high (10 to 63 per thousand compared with 0·8 to 1·2 notified cases of pneumonia per thousand in England and Wales). Manganese, in the form of manganese dioxide dust and of a solution of manganese chloride, was introduced into rats by intratracheal injection and the animals were killed from a few minutes to 18 months later. Within 15 minutes of exposure to manganese dioxide there were marked changes in the bronchial epithelium. In 24 hours an intense mononuclear infiltration of the alveoli was seen, followed in some cases by a granulomatous reaction. After injection of manganese chloride many animals died of pulmonary oedema, but the alveolar infiltration was less intense. *C. Bruce Perry*

2663. **The Morphology of Bauxite-fume Pneumoconiosis**
J. P. Wyatt and A. C. R. Riddell. *American Journal of Pathology* [*Amer. J. Path.*] **25**, 447–465, May, 1949. 8 figs., 18 refs.

The morphology of the lungs is described in 6 fatal cases of a new type of pneumoconiosis found among furnace attendants making an aluminium abrasive preparation. The changes, which are non-specific, are of a chronic inflammatory nature and include fibrosis, endarteritis, proliferation of the alveolar epithelium, emphysema, and bronchiolectasis. Acute infections were frequent in the cases studied, but played no part in the progression of the condition, and the occurrence of active tuberculous caseous foci appeared to have been coincidental. The pulmonary fibrosis was septal and interlobular and not of the carnification type; it was often hyalinized. There were no granulomatous foci (as with beryllium). Silica, as well as aluminium, had been present in the fumes inhaled, but, because of the absence of nodular fibrosis, was thought not to be responsible for the condition, which was attributed principally to the aluminium. *D. M. Pryce*

2664. **Changes in the Lungs Produced by Natural Graphite**
H. E. Harding and G. B. Oliver. *British Journal of Industrial Medicine* [*Brit. J. inudstr. Med.*] **6**, 91–99, April, 1949. 10 figs., 14 refs.

Graphite is a substance of variable composition; only two-thirds of it may be carbon and it contains quantities of crystalline silica (8 to 18·6% in the samples tested). A considerable risk from dust exposure occurs in the grinding of natural graphite and this can lead to fatal pneumoconiosis. Necropsy on 3 men who had worked in graphite dust for 16, 19, and 22 years respectively, revealed anthraco-silicotic changes in the lungs similar to those seen in coal workers. Radiographs of men employed at a factory showed no abnormality in those with less than 10 years' exposure to graphite and in only one case of less than 20 years' exposure. In 13 there were varying degrees of reticulation and nodulation similar to that seen in the pneumoconiosis of coal workers. Graphite was injected into the bronchi of groups of 3-month-old rats and 6 to 9 months later the animals were killed; pigment was found to be distributed throughout the lungs in small black areas. There was a foreign-body reaction around the pigment, and an increase in reticulin fibrils with slight collagenous fibrosis. *C. Bruce Perry*

2665. **Tuberculosis in Industry: An Epidemiological Study. Preliminary Report**

A. STEWART and J. P. W. HUGHES. *British Medical Journal* [*Brit. med. J.*] **1**, 926–929, May 28, 1949. 2 refs.

This report deals with the prevalence of pulmonary tuberculosis in the boot and shoe industry, a matter which was considered 34 years ago in the first report of the Medical Research Committee. Various modern methods of investigation were used, including a comparison of the physique of boot and shoe operatives with that of other workers, miniature mass radiography surveys, a study of the distribution of cases according to size of factories. The conclusions in several respects are in accord with those of the earlier report. The first mass radiography survey in Northamptonshire, the centre of the boot and shoe industry, demonstrated a statistically significant excess of newly discovered cases of active pulmonary tuberculosis in the industry, but there was no evidence of any excess of either heart disease or other respiratory conditions. Service recruiting records indicated that there were more men of subnormal physique in the industry than in most occupations. Further, shoemaking tends to be an industry with a family tradition. The problem to be solved was whether infection was carried to the factory from infected families, or from the infected factory to subnormal operatives. When the factories were grouped according to the size of the factory population, somewhat unexpectedly the incidence of newly discovered cases was found to increase with the size of the working population, as shown in the table below.

Size of Working Population	Pulmonary Tuberculosis Rate per 1,000
1–100	3·1
101–200	5·2
201–350	6·2
351–600	7·4
over 600	10·1

Such factors as age and sex of workers, occupation, regional distribution of factories, and factory conditions, including ventilation and lighting, were carefully considered and rejected as contributing influences. The conclusion seems to be that the industry is one in which operatives contract the infection from their fellows; the larger the population the greater the probability that one or more infected persons will be present among the population. No evidence was found of any specific industrial hazard. Another " infected " industry is the clothing trade [and the printing industry]; investigation on the lines so successfully adopted in the present report is called for.

[An effort should therefore be made to eliminate open cases of tuberculosis from the factories. Here is evidence that, although tuberculosis may be regarded as a social disease, it is primarily an infectious disease which can be eliminated only by controlling the infection.]

E. L. Collis

2666. **A New Pulmonary Mycosis.** (Une nouvelle toxomycose pulmonaire)

L. KÖZÉPEZY. *Archives des Maladies Professionelles* [*Arch. Mal. prof.*] **10**, 130–139, 1949. 7 figs., 5 refs.

The Indian millet (*Sorghum vulgare*), which is widely grown in the Csanád Department of Hungary, suffered severely in 1947 from a blight caused by a parasitic fungus identified as *Sphaceloteca sorghi* Line-Clinton. The prevalence of the fungus was considered to be due mainly to the poor condition of the soil after the years of war, plants grown on poor soil having but a feeble resistance to fungus invasion. There is no previous record of any illness in animals or man caused by this blight, but in 1947 pulmonary disease caused by inhalation of the fungus while threshing the millet was observed in 49 labourers. Some 30 others were affected, but recovered without medical attention. The irritating black dust from the threshing machines caused most of the labourers to cough, but the more serious symptoms only appeared after 3 or 4 weeks of the work and affected primarily the mechanics and those who fed the threshing machines. The varying incidence and severity of these symptoms suggested individual predisposition in some cases. Those affected suffered from persistent cough and became more and more fatigued, anaemic, and unable to take their food. Eventually there was a sudden rise in temperature, which was preceded by marked dyspnoea accompanied by prostration and was considered to be due to secondary infection. Some of the patients recovered in 10 to 15 days with simple treatment, others took from 6 to 8 weeks to recover; while a third group of patients developed pulmonary fibrosis, sclerosis, and chronic, incapacitating bronchiectasis. One of the patients died.

Several cases are described in detail (including one in which the patient had a history of pulmonary illness after working with blighted millet in 1942 and recurring in successive years thereafter) and a general account is given of the clinical course and the pathological and radiological findings. From the early acute stage with cough as the only symptom, the disease passed through successive stages of congestion, oedema, and atelectasis of the lungs to the stage of resolution and recovery, or to that of persistent dilatation of the bronchioles with bronchiectasis and sclerosis. Radiologically, the upper lobe of the right lung was most commonly affected, the apices were almost always clear, and there were only slight opacities in the lower lobes. The clinical condition closely resembled that of an acute exudative pulmonary tuberculosis, but the sputum in every case was negative for tubercle bacilli and in most cases was found to contain two varieties of fungus, *Aspergillus niger* and *Mycotoruloides*. By cutaneous tests it was decided that *Mycotoruloides* was the pathogenic agent. Treatment included the control of secondary infection by means of sulphathiazole or penicillin, and the relief of respiratory distress. In one case haemoptysis occurred and could only be controlled by phrenectomy and repeated transfusion. Prophylactic measures are suggested, both to control the blight and to protect the labourers.

M. A. Dobbin Crawford

Genetics

2667. **The Cytogenetic Effect of Sonic Energy Applied Simultaneously with *X*-rays**
A. D. CONGER. *Proceedings of the National Academy of Sciences, Washington* [*Proc. nat. Acad. Sci., Wash.*] **34**, 470–474, Oct., 1948. 9 refs.

Inflorescences of a clone of *Tradescantia paludosa* were subjected to simultaneous *x*-ray (250 r) and sonic (9,100 cycles per second) treatment, the latter continuing for five minutes after irradiation had ceased. The yield of chromosomal aberration induced by *x* rays and sonic energy in six experimental series was 1·3 times higher than the yield after *x*-ray treatment alone. Sonic energy alone did not produce detectable aberrations. The increase in yield is probably due to an increased movement of the fragments of chromosomes; this increase, caused by the sonic treatment, results in a decrease in the number of normal restitutions, which otherwise would not be detected. *H. Kalmus*

2668. **The Teaching of Michurin and Lysenko and some Questions on Constitution and Inheritance in Pathology.** (Учение Мичурина-Лысенко и некоторые вопросы конституции и наследственности в патологии)
P. D. GORIZONTOV. Архив Патологии [*Arkh. Patol.*] **11**, No. 1, 3–17, Jan.–Feb., 1949. 23 refs.

Those geneticists who hold the view that heredity is independent of environment and is vested in the germ plasm do so in the face of increasing evidence to the contrary. For example, it is well known that an incised leaf of begonia laid on the ground will give rise to a complete new plant with flowers and seed, that is, " the immortal carrier of heredity arises out of mortal somatoplasm ". This and a host of later observations have conclusively shown that, in the words of Lysenko, " there is not and cannot be any organ of heredity ". Numerous observations point to the influence that environment has over heredity. In widely separated parts of the world representatives of the most varied groups of plants show most astonishing similarity, provided that local condition are similar. Tower has succeeded in changing the colour of the Colorado beetle by varying external temperatures. Vladimirsky quotes many examples of inheritable variations in the furs of animals obtained by changing temperatures. Michurin has shown that it is not only possible to change the heredity of plants, but that these changes can be made to suit the requirements of man. *Bacillus prodigiosus* forms red pigment at room temperature. If the temperature is raised to 30 to 35° C. no pigment is formed. If the warm culture is then transferred to a lower temperature it loses the ability to form pigment for a considerable time. Pasteur and Metchnikoff were able to attenuate the virulence of micro-organisms.

Geneticists either overlook inconvenient observations entirely or else invoke so-called " idiokinetic factors ", the latter being inscrutable causes of variations in the germ plasm. These idiokinetic factors, together with arbitrary definitions and involved nomenclature, serve only to obscure the real issues. Bogomoletz asked pertinently: " What are these idiokinetic factors which remain immune to all influences of material environment ? If they are not material, then it is impossible not to doubt their existence. But if they are built of living matter, then how can they escape the effects of hunger, exhaustion, alcoholism, syphilis, or tuberculosis on their carrier? "

A fundamental contradiction exists in the genetical conception of human heredity. It is emphatically denied that acquired characteristics can be inherited, yet on the other hand more and more diseases, or at least susceptibilities to disease, are added to the long list of hereditary conditions. Some geneticists have even written of the tuberculosis and syphilis genes.

The social implications of formal genetics are serious. They amount to no less than an acceptance of the laws of natural selection in human society, leading to the not undesirable elimination of the unfit and the " purification " of society. This may serve as " scientific " justification of the brutality of life under capitalism. Some reactionary geneticists have gone even further in inventing a new " science " of eugenics, a science which reduces man to the level of cattle. In the Soviet school of biology, the fact of heredity is fully recognized, but its definition is decisively altered. Thus Lysenko defines it as the quality of the living organism to require definite conditions for its development and to react in a definite way to these or other conditions. This concept allows for a full interaction between the individual, the species, and the environment. It is recognized that some changes in environment may produce changes in heredity, provided that the sex cells have been affected in the first place. It is, however, freely admitted that heredity is on the whole conservative. Pathological changes may also be inherited, though this is rare; detrimental changes are not as a rule fixed in the species; they tend to disappear.

Not all hereditary traits reveal themselves in any one individual. Their appearance or non-appearance also depends on appropriate environmental conditions. In theory, it is therefore not impossible to prevent such an appearance of harmful qualities by a suitable modification of the environment.

Inheritance does often follow so-called " Mendelian " laws, but these laws have no connexion whatever with the chromosomal mechanism of the sex cells, since identical inheritance phenomena were observed in the hybridization of plants. Moreover, it is apparently possible to modify these laws, particularly in early life and under circumstances of " shaken heredity ", as described by Lysenko.

The question of the inheritance of local changes in tissues must be treated in the light of the relation between the local and the general factors of the living body. Abnormal mutations in cells may be produced locally, as in experimental carcinogenesis, yet in some cases local processes may be subordinated to and inhibited by general or correlational factors. For example, prostatic cancer may be sensitive to hormonal treatment.

It is not disputed that constitutional factors exist and play an important part in the causation of disease, but much of the interpretation hitherto placed on the accumulated evidence needs revision. The sex linkage of haemophilia, for example, cannot be regarded as fully established for the following reasons: (1) A certain focal incidence in the appearance of that disease has been reported by some workers. (2) It occurs occasionally in cases with no previous family history. (3) It is possible to explain the sex incidence of clinical haemophilia by the effect of hormonal influence without reference to a hypothetical sex linkage. (4) A condition resembling haemophilia has been produced experimentally by the administration of heparin in animals. Similarly, although it is known that membership of blood groups is inherited in accordance with Mendelian laws, there is no good reason for linking that inheritance with chromosomes or genes.

The consideration of the problems of immunity is equally pertinent. Bogomoletz wrote: "The same constitutional phenomena may be hereditary, congenital, or acquired. The phenomena of immunity are an excellent proof of this statement". Ehrlich has shown that acquired immunity against certain poisons may be inherited. Ott has been able to show that increased skin sensitivity to these poisons may also be inherited.

Medicine is at present regarded as helpless when confronted with hereditary and constitutional diseases. This defeatism is rooted in the unwarranted assumptions of formal geneticists. Soviet biology offers a new and hopeful approach for an attack on this problem through the study of the exact part played by environment in the causation of such diseases and research into the effects of planned changes in environment. *L. Crome*

2669. **Congenital Blindness (Pseudoglioma) occurring as a Sex-linked Developmental Anomaly**
W. M. G. Wilson. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **60**, 580–584, June, 1949. 4 figs., 5 refs.

This paper records the occurrence of congenital pseudoglioma (non-attachment of the retina) in a family group of Indians from Manitoulin Island, Ontario, Canada. Altogether 10 males have been affected in the past three generations; in addition, a blind female occurred two generations previously. The most remarkable group within the pedigree involves an Indian woman who, by 5 different men (2 Indians, 2 Europeans, and a "quarter-breed"), had 6 affected sons, one normal son, and 9 normal daughters; of these, all but one of the affected sons have been examined, and histological preparations of enucleated eyes from 3 of them have been examined. Two of these are remarkably alike; the third, however, differs somewhat, but this eye had been removed at a much later stage. It is assumed that pseudoglioma is due to a sex-linked recessive gene, as there are 10 affected males who inherited the condition through normal mothers; the affected female may have had a different kind of blindness. Alternatively, the gene might have shown semi-dominance in a heterozygous woman, as sometimes happens in colour-blindness.

[While the explanation given by the author is probably correct, it cannot be regarded as proven. None of the affected males left any offspring; hence, as it is not known whether the condition can be transmitted directly from father to son, sex-limitation must be considered a possible alternative explanation.] *H. Grüneberg*

2670. **Retinitis Pigmentosa Associated with Cystinuria. Two Uncommon Inherited Conditions Occurring in a Family**
W. D. W. Brooks, M. A. Heasman, and R. R. H. Lovell. *Lancet* [*Lancet*] **1**, 1096–1098, June 25, 1949. 6 figs., 7 refs.

The authors describe a family of 6 children amongst whom both retinitis pigmentosa and cystinuria were found. The mother had neither disease, and the same is presumed in respect of the father, who died young. The parents were third or fourth cousins and, so far as could be ascertained, all their brothers and sisters were normal. Of their six children, two brothers had neither disease; one brother and one sister (who was fully investigated by the authors) had both; one sister had cystinuria, but "no visual disturbance" [apparently she had not been examined ophthalmoscopically] and one brother (missing since 1939) had retinitis pigmentosa, but had not been examined for cystinuria. On the basis of these facts the authors conclude that "the retinitis pigmentosa in this case and probably the cystinuria are autosomal recessive characters. The gene for cystinuria is probably located on a different chromosome pair from that of retinitis pigmentosa."

[It seems to the abstracter that these conclusions are open to criticism. In the first place, although the authors mention the occurrence of retinitis pigmentosa with deafness as a discrete syndrome due to a single gene, they do not consider the possibility that retinitis pigmentosa with cystinuria might be a similar syndrome, not hitherto described, of which not all the constituents are regularly manifested. Secondly, even if we follow the authors and assume two genes, it is by no means likely that these genes are located in different pairs of chromosomes. For while one gene might be handed down from a common ancestor through two lines of descent to segregate out in the sibship described, it is most improbable that a second gene, independent of the first, should be handed down in the same line of descent. It becomes more likely if the two genes are linked, and the likelihood is greatest if the two genes constitute in fact a single pleiotropic gene. It is thus suggested that the facts presented, so far from indicating the segregation of two independent genes, point strongly in the opposite direction, that is, towards either two linked genes, or a single gene with pleiotropic effects.] *H. Grüneberg*

Physiology and Biochemistry

2671. **The Iron Reserve of a Normal Man**
M. HYNES. *Journal of Clinical Pathology* [*J. clin. Path.*] **2**, 99–102, May, 1949. 3 figs., 3 refs.

Working in the Department of Medicine, Cambridge University, the author studied the iron reserve in a 37-year-old man weighing 63 kg. who had lived for 16 months on a normal English civilian diet. He was bled daily 90 minutes after breakfast, anaemia being established by 2 blood withdrawals of 800 and 900 ml. respectively; 2,750 ml. blood was removed in the 136 days of the experiment by venepuncture without any venous compression and with use of Wintrobe's dry oxalate mixture as anticoagulant, pipettes being filled at once before sedimentation could begin. All estimations were duplicated, haemoglobin being estimated photoelectrically as oxyhaemoglobin. Serum and plasma specific gravities were measured by the copper sulphate technique of Van Slyke. The daily rate of haemoglobin regeneration was calculated from the best-fitting polynomials to the observed haemoglobin levels in each period of the experiment. There were relatively small day-to-day fluctuations in haemoglobin level, accompanied by changes in haematocrit value and plasma specific gravity, with a day-to-day variation of $\pm 5\%$ in plasma volume. Such fluctuations were excluded from the calculation of haemoglobin regeneration by statistical fitting of curves to data. After the two large venesections the fall in haemoglobin corresponded to 5·3 and 5·5 litres respectively, the haemoglobin level falling progressively for a few days after venesection, during which time a compensatory increase in plasma volume occurred. The daily utilization of iron for haemoglobin regeneration in excess of that required for the normal replacement of effete erythrocytes fell to a minimum on the 45th day and remained constant thereafter, suggesting that the subject's iron reserve was finally exhausted at that time. The calculations by which the iron reserve was worked out are given and the value arrived at is about 600 mg. The mean corpuscular haemoglobin concentration and mean corpuscular volume, after an initial rise, fell progressively throughout, the rise and fall both being statistically significant. When, after the 123rd day of the daily withdrawal of 20 ml. blood, full doses of iron were given by mouth, the rate of haemoglobin regeneration rose steeply after an interval. All this suggested that the supply of iron was the limiting factor in blood formation. The reticulocyte count rose from 0·2% at the beginning of the experiment to 0·4% when haemoglobin regeneration was maximal and was only 0·1% when the haemoglobin level was falling; when iron was administered the reticulocyte count rose to 0·7%. An iron reserve of 600 mg. was enough to replace one-fifth of the subject's normal haemoglobin content. The British diet affords about 4 mg. iron daily for haemoglobin synthesis in addition to the 1 mg. needed to replace the daily excretion of iron in bile and urine. This 4 mg. is only sufficient to replace a loss of 8 ml. blood daily by haemorrhage; moderate menorrhagia might require for replacement more than the available 4 mg. of extra iron. Transfusion donations of 450 ml. could be made 5 times yearly without depleting the iron reserve. *Walter H. H. Merivale*

CIRCULATORY SYSTEM

2672. **On the Question of the Reflex Mechanism of Respiratory Arrhythmia.** (Zur Frage der reflektorischen Steuerung der respiratorischen Arrhythmie)
K. MECHELKE and H. J. MEITNER. *Zeitschrift für Kreislaufforschung* [*Z. KreislForsch.*] **38**, 268–283, May, 1949. 7 figs., 29 refs.

On the basis of their own observations and those of other workers, the authors explain the mechanism of respiratory arrhythmia as a purposeful interaction of the Bainbridge and depressor reflexes. The increased filling of the auricle and large veins during inspiration leads to an increase of the heart rate; the larger stroke volume resulting from the increased venous filling, after an interval representing the time of circulation through the lungs, causes an increase in arterial pressure which, through stimulation of the presso-receptors, excites the Bainbridge and depressor reflexes and results in bradycardia and a fall in arterial pressure. Such a mechanism would explain certain alterations in the usual relation between phase of respiration and heart rate, and its occasionally observed reversal. Incidentally, the 5 patients studied in connexion with the present work had nodal rhythm in the phase of bradycardia. *B. Samet*

2673. **Starling's Law and *X*-ray Density Changes of Heart Shadow**
G. C. RING, C. R. MICHIE, and M. J. OPPENHEIMER. *American Journal of Physiology* [*Amer. J. Physiol.*] **156**, 339–344, March, 1949. 4 figs., 14 refs.

2674. **Respiratory Function and Blood Flow in the Bronchial Artery After Ligation of the Pulmonary Artery**
W. E. BLOOMER, W. HARRISON, G. E. LINDSKOG, and A. A. LIEBOW. *American Journal of Physiology* [*Amer. J. Physiol.*] **157**, 317–328, May, 1949. 6 figs., 17 refs.

The authors have demonstrated in dogs that after ligation of a main pulmonary artery under sodium pentobarbitone anaesthesia the lung can carry on the function of respiration, its capacity to absorb oxygen gradually increasing over a period of months. There is considerable enlargement of the bronchial vascular bed, which is supplied by collateral branches from enlarged oesophageal and pericardiophrenic vessels, and blood from the bronchial vessels reaches the capillaries of the

alveoli. Although in the intact lung of the dog and of man precapillary anastomoses do not normally exist between the bronchial and pulmonary arteries, reference is made to anatomical studies which have demonstrated the opening up of such anastomoses in cases of congenital pulmonary stenosis (Hales and Liebow, *Bull. int. Ass. med. Mus.*, 1948, **28**, 1) and bronchiectasis (Liebow *et al.*, *Amer. J. Path.*, 1949, **25**, 211). Most of the increase in the bronchial blood flow occurs within the first few weeks of ligation of the pulmonary artery, and after the fourth month the flow usually exceeds 1 litre per sq. m. of body surface per minute. *A. I. Suchett-Kaye*

2675. **Antithrombin and Heparin in Human Blood**
T. A. LOOMIS. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 631–636, May, 1949. 4 figs., 11 refs.

This paper is concerned with the further identification of a factor (proantithrombin) in human plasma the action of which, in the presence of heparin, results in the formation of antithrombin. This factor is present in the plasmin fractions obtained by ammonium sulphate fractionation, and in Fraction III-3 obtained by alcohol fractionation. It is rapidly inactivated by exposure to a temperature of 70° C. and has the characteristics of Howell's proantithrombin. *A. W. H. Foxell*

2676. **A Factor in Serum which Accelerates the Conversion of Prothrombin to Thrombin. II. Its Evolution with Special Reference to the Influence of Conditions which Affect Blood Coagulation**
B. ALEXANDER, A. DE VRIES, and R. GOLDSTEIN. *Blood* [*Blood*] **4**, 739–746, June, 1949. 3 figs., 15 refs.

2677. **A Factor in Serum which Accelerates the Conversion of Prothrombin to Thrombin. III. Its Relationship to the Coagulation Defect of Thrombocytopenic Blood**
B. ALEXANDER and A. DE VRIES. *Blood* [*Blood*] **4**, 747–751, June, 1949. 16 refs.

RESPIRATORY SYSTEM

2678. **Some Observations on the Co-ordination of Diaphragmatic and Rib Movement in Respiration**
H. HERXHEIMER. *Thorax* [*Thorax*] **4**, 65–72, March, 1949. 2 figs., 9 refs.

This investigation was designed to demonstrate the relative parts played by the diaphragmatic and the intercostal muscles in varying phases of respiration. Simultaneous tracings from normal subjects were made with a spirometer and a thoracograph. The latter instrument consists essentially of a steel band placed round the chest usually at the level of the third interspace. It measures circumference changes in terms of the corresponding air exchange. The volume of total air exchange, as shown by the spirometer, depends usually upon both costal and diaphragmatic movement. By thus separately recording the costal element, it is possible by comparison of the tracings to estimate the relative contribution of each element. For example, if only the diaphragm were being used, the whole of the spirometer reading would be due to its action and no rib movement would be shown on the thoracograph.

As part of the investigation a subject was told to hold his breath at a certain point in inspiration, subsequently continuing to maximum inspiration while keeping his eye on the spirometer. He was instructed to hold his breath again during the expiratory phase as soon as the previous spirometer reading was reached. As before, the interruption was to continue for long enough to mark the two tracings. By reading the synchronized tracings it became apparent which portions of the complemental air were made by costal action and which by the diaphragm. The reserve air was similarly assessed in the course of interrupted maximum expiration.

With this technique it was seen that the proportion of costal to diaphragmatic movement changed throughout the cycle. The following observations were made: (1) In the standing position quiet breathing is often purely diaphragmatic, the costal muscles taking some part when the subject lies down. (2) Complemental air is moved predominantly by costal muscles, reserve air predominantly by the diaphragm. This tendency becomes less pronounced when the patient is supine. (3) It follows that an increased reserve air indicates a low-level diaphragm of good mobility. (4) After the inspiratory or expiratory limit has been reached by the concerted action of diaphragm and ribs, the diaphragm starts the reverse movement, while the ribs move only a little; later they join in and near mid-position take over most of the action. (5) Raising of the diaphragm leads to an increase in chest circumference during quiet breathing and therefore has little effect on the vital capacity.
I. McD. G. Stewart

2679. **Respiratory Quotient and Regulation of Respiration.** (Respiratorischer Quotient und Atmungsregulation)
R. MOND. *Pflügers Archiv für die Gesamte Physiologie* [*Pflüg. Arch. ges. Physiol.*] **251**, 255–261, 1964. 1 fig., 11 refs.

2680. **The Combined Influence of Carbon Dioxide Excess and Oxygen Lack on the Respiratory Volume.** (Über das Atemvolumen bei der gleichzeitigen Einwirkung von Kohlensäureüberschuss und Sauerstoffmangel)
K. GOLLWITZER-MEIER. *Pflügers Archiv für die Gesamte Physiologie* [*Pflüg. Arch. ges. Physiol.*] **251**, 335–343, 1949. 3 figs., 15 refs.

2681. **The Effect of Breathing Oxygen at Atmospheric Pressure on Tissue Oxygen and Carbon Dioxide Tensions**
H. J. TAYLOR. *Journal of Physiology* [*J. Physiol.*] **108**, 264–269, May 15, 1949. 2 figs., 13 refs.

2682. **Measurement of Intrapulmonary Pressure During Exertion.** (Mesure de la pression intrapulmonaire au cours de l'effort)
A. BASSET and J. F. JOLIET. *Comptes Rendus des Séances de la Société de Biologie* [*C.R. Soc. Biol., Paris*] **143**, 482–485, April, 1949. 1 fig., 3 refs.

2683. **The Metabolic Cost of Passive Cycling Movements**
J. A. SAUNDERS. *Journal of Physiology* [*J. Physiol.*] **108**, 353–358, May 15, 1949. 8 refs.

NUTRITION

2684. **Vitamin D_2 Poisoning in Adults.** (Vigantolvergiftung beim Erwachsenen)
H. WAGNER. *Virchows Archiv für Pathologische Anatomie und Physiologie* [*Virchows Arch.*] **316**, 666–688, 1949. 5 figs., bibliography.

The case reported in this article appears to be the first of fatal hypervitaminosis D in the German literature; it has already been more briefly reported and further articles on the clinical aspects and vascular lesions are planned. The present article deals chiefly with the visceral lesions. The patient was a woman of 50 who had suffered from lupus vulgaris for 16 years. Calcium and non-protein nitrogen levels in the blood and urine were normal on her admission. She was given vitamin D_2 in the form of " vigantol forte " [an irradiated ergosterol and presumably not the material of the same name which in the early days of irradiated ergosterol was notorious for its toxicity] in 10 mg. doses with diminishing frequency (the Charpy system) over 5 weeks, a total of 150 mg. being administered. Uraemia then appeared, the non-protein nitrogen level reaching 293 mg. per 100 ml. and the calcium level 14 mg. per 100 ml. of blood. The patient's condition began to improve under treatment but after 12 days she died of pulmonary embolism.

The aorta showed marked medial calcification, other large arteries very little. In many areas of lung there was calcification of the alveolar walls and of the pulmonary arteries. The kidneys showed tubular degeneration, with regeneration and very little calcification. It is pointed out that the blood pressure had not risen but that the sodium chloride level in blood had fallen, both indications of a tubular lesion. Many heart muscle fibres and many coronary arterioles were calcified. There was osteoporosis; it is suggested that this may be a direct effect of hypervitaminosis D [but as there was narrowing of bone trabeculae and no active osteoclasis it is difficult to suppose that it could have been a recent event]. No relevant changes were seen in other organs. The whole condition had the appearance of a genuine hypervitaminosis D in which the most important change was an almost pure tubular lesion of the kidney which was in process of recovery at the time of death. [The comparatively brief description of the kidney lesions shows no evidence of acquaintance with recent work on the tubular nephroses.] *Bernard Lennox*

2685. **Influence of Various Levels of Thiamine Intake on Physiologic Response. VI. Oxygen Consumption**
W. W. TUTTLE, M. WILSON, K. DAUM, and H. RHODES. *Journal of the American Dietetic Association* [*J. Amer. diet. Ass.*] **25**, 322–329, April, 1949. 4 figs., 6 refs.

The oxygen consumed by 12 normal young women during 1 minute of work on a bicycle ergometer and the next 10 minutes of resting was measured weekly or twice weekly, the work being regulated to a constant rate of 1,250 kg. m. per minute. During the given " work-and-recovery " period the subjects breathed out of and into a spirometer mounted on an electrically driven extension kymograph which was set to revolve at 30 mm. per minute; as even an enlarged spirometer did not hold enough oxygen for the needs of the experiment, the tank was refilled quickly during the recovery period, usually 2 to 4 minutes after the cessation of work, without interruption of the experiment. An increased consumption of oxygen (and therefore a loss of efficiency) occurred when the dietary intake of aneurin (thiamin) was restricted to 140 μg. daily for 6 weeks and also when it was restricted to 200 μg. daily for 19 weeks, although in the latter case the effect took longer to appear. Improved efficiency was observed in all but one subject on an aneurin intake of 625 μg. daily, and in all subjects on an intake of 1,000 μg. daily. Considerable time was required to recover from the loss of work efficiency caused by low aneurin intake. *Joseph Parness*

2686. **Influence of Various Levels of Thiamine Intake on Physiologic Response. VII. Thiamine Requirements and their Implications**
K. DAUM, W. W. TUTTLE, and M. WILSON. *Journal of the American Dietetic Association* [*J. Amer. diet. Ass.*] **25**, 398–404, May, 1949. 49 refs.

This paper reviews the results of the investigations published in the first six papers of the series (*Abstracts of World Medicine*, 1949, **6**, 8, 137, 393), and, in particular, relates these results to those of other workers. Some of the earlier work must be interpreted with caution, because the experiments often covered short periods and the diets were very different from those normally consumed. The experiments of the present authors extended over 5 months, and the diets, apart from their low content of aneurin, were quite normal.

The authors point out that the requirements for any nutrient vary with the individual, and are influenced by such factors as age, physiological stress, and the possibility of adaptation. Their own results suggest that the requirement of aneurin for healthy young adults is about 0·63 mg. daily, or 0·25 to 0·30 mg. per 1,000 Calories. The normal American dietary would supply approximately this amount only if care were taken to avoid any unnecessary loss in cooking; the use of enriched (fortified) bread and flour would increase the average daily intake by about 0·20 mg. daily. *J. Yudkin*

2687. **The Utilization of Nicotinic Acid by Pregnant Women**
E. I. FRAZIER, T. PORTER, and M. J. HUMPHREY. *Journal of Nutrition* [*J. Nutrit.*] **37**, 392–410, April, 1949. 2 figs., 15 refs.

This study was carried out on 7 primigravidae, 42 pregnant women selected at random from those attending a clinic, and 12 non-pregnant women. The dietary intake of nicotinic acid and the urinary excretion of N′-methyl nicotinamide were estimated in each of the women. In addition, in the first group the acid-hydrolys-

able fraction (free nicotinic acid, nicotinuric acid, and nicotinamide) and the response to a test dose of 50 mg. of nicotinamide were measured, and in the last group the response to the same test dose was determined.

The level of excretion of the acid-hydrolysable fraction was constant and not related to the intake; that of the methyl derivative was also not related to intake, but it increased during pregnancy and was higher in the pregnant than in the non-pregnant women. The response to the test dose tended to rise slightly during pregnancy. The most interesting observation was that there was an inverse relationship between the intake of the vitamin and the response to the test dose: the higher the intake, the lower was the proportion of the test dose excreted. This is contrary to what is normally expected in response to test doses of the water-soluble vitamins. It is suggested that this, and the increasing excretion of the N′-methyl nicotinamide as pregnancy proceeds, might be explained as in some way reflecting an increasing utilization of the vitamin with the increasing metabolism of the maternal tissues.

J. Yudkin

2688. **Effect of Pressure Cooking on Vitamin C Content of Vegetables**

G. M. CHAPPELL and A. M. HAMILTON. *British Medical Journal* [*Brit. med. J.*] **1**, 574–575, April 2, 1949. 1 ref.

The authors have compared the loss of vitamin C in vegetables cooked in a 7-pint (4-litre) pressure cooker and by the method recommended by the Ministry of Food—using only as much water as is necessary to prevent burning of the saucepan, bringing it to the boil, and cooking the vegetable as briefly as possible. One advantage of the use of the pressure cooker is that only half as much water is needed as for cooking in an ordinary saucepan. In six of the vegetables—cauliflower, broccoli, winter cabbage, new carrots, turnips, and swedes—the pressure cooker retained from 3 to 28% more of the vitamin C than did the saucepan. In the other four—spring cabbage, broad beans, old carrots, and spinach—the results were about the same. In all the experiments the retention was slightly greater in the cooker (66% vitamin C) than in the saucepan (58·5%). Another great advantage of the pressure cooker is that the vegetable quickly breaks up if overcooked, so the housewife soon learns not to do this; whereas, with the saucepan, overcooking with a large volume of water does not affect the appearance or palatability of the vegetable, although much more of the vitamin is lost.

T. E. C. Early

See also Section Digestive Disorders, Abstract 2910.

2689. **Parenteral Nutrition. VIII. The Vasodepressor Activity of Soybean Phosphatide Preparations**

R. P. GEYER, D. M. WATKIN, L. W. MATTHEWS, and F. J. STARE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 688–698, May, 1949. 8 refs.

Various fractions of soya bean phosphatides have been used as stabilizers in fat emulsions for intravenous feeding and an emulsion containing 15% of coconut oil with 3% of fraction B(F-2) (Geyer *et al.*, *J. Lab. clin. Med.*, 1948, **33**, 163) has been administered intravenously to animals without adverse effect being noted other than a moderate anaemia of normocytic type. In a few preliminary observations in man, however, a fall in arterial blood pressure occasionally followed the intravenous injection of the emulsion. On further investigation, a marked fall in blood pressure occurred when even small quantities of the emulsion were injected intravenously into the cat, although its effect was slight in the dog and absent in the rat and rabbit. The vasodepressor action was found to be present in the commercial preparation of soya bean phosphatides from which the fraction was obtained; it was not present in the freshly made preparation of soya bean phosphatides, but developed when it was allowed to stand in contact with air. The vasodepressor substance could not be identified with any of the known phosphatides or their simple degradation products. It was possible to concentrate the vasodepressor substance considerably, and also to prepare phosphatide fractions low in vasodepressor activity, but these were either poor emulsifying agents or, if suitable as emulsifying agents, they underwent changes on autoclaving which gave rise to toxic effects. It has not yet been possible to prepare a depressor-free phosphatide fraction which would also be a suitable emulsifying agent. It is considered desirable that tests of fat emulsions intended for clinical use should be carried out in several species of animal, including the cat.

Joseph Parness

2690. **Parenteral Nutrition. IX. Fat Emulsions for Intravenous Nutrition in Man**

G. V. MANN, R. P. GEYER, D. M. WATKIN, and F. J. STARE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 699–712, May, 1949. 4 figs., 5 refs.

Fat emulsions for intravenous feeding containing 15% of coconut oil or corn oil were stablized with a combination of the B(F-2) fraction of soya bean phosphatides at a concentration of 0·5%, which produced minimal vasodepressor effect in the cat (see Abstract 2689), and a polyglycerol ester at a concentration of 1%. Intravenous injection of the emulsions into cats, rats, and dogs produced no adverse effect other than a moderate anaemia of normocytic type. The emulsion (coconut oil) was then injected cautiously into 6 appropriate human subjects in hospital. No adverse effects were noted in the patients as a result of intravenous injections given on various occasions within 25 days of preparing the emulsion; during this time amounts up to 600 ml. daily were given, while one patient received 300 ml. daily for 8 successive days. After the emulsion was 25 days old, however, pyrexial reactions occurred after its injection and it was also found to be strongly pyrogenic in rabbits, although sterile on culture. Additional studies confirmed the presence of pyrogens at this stage, but the mechanism of their slow development is not yet known; it appears to be non-bacterial in origin and is accelerated by repeated autoclaving of the emulsion.

Joseph Parness

Pharmacology and Therapeutics

2691. **Influence of " Nembutal ", " Pentothal " (Thiopentone), and Pentothal-Tubocurarine on Respiration and Circulation.** (Influences du nembutal, du pentothal et du pentothal-tubocurarine sur la respiration et la circulation sanguine)
J. R. VERSTRAETE. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **78**, 283–300, Feb., 1949. 6 figs., 21 refs.

The author carried out experiments designed to test the effects of different anaesthetic procedures on the blood pressure, the reflex regulation of blood pressure, and the respiration. In dogs under light morphine-ether anaesthesia the aortic arch was denervated so that reflex regulation of blood pressure depended upon the carotid sinuses only; the reflex was tested by occlusion of both common carotid arteries which caused a large rise in blood pressure. Respiration was recorded by means of a pneumogram. Injection of clinical doses of " nembutal " (pentobarbitone) in the above preparation depressed the blood pressure and its reflex control only slightly, but greatly depressed respiration. " Pentothal " (thiopentone) caused a transient inhibition of respiration but did not affect the blood pressure or its reflex control. The combination of tubocurarine in clinical doses with pentothal increased the respiratory depression and, as might be expected, large doses of tubocurarine depressed the blood pressure and its reflex regulation and paralysed the respiration. Chloralose combined with pentothal depressed the respiration and lowered the blood pressure slightly without affecting its regulating mechanism. [The author's summary is rather confusing: it fails to mention the morphine-chloralose-pentothal combination but describes the effects of morphine-chloralose-nembutal, of which the paper itself makes no mention.]
John R. Vane

2692. **The Effect of Therapeutic Doses of Aspirin on the Acid–Base Balance of the Blood in Normal Adults**
H. R. FARBER, M. J. YIENGST, and N. W. SHOCK. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **217**, 256–262, March, 1949. 3 figs., 17 refs.

Aspirin (acetylsalicylic acid) was given in hourly doses of 1·3 g. to 10 healthy males aged 14 to 40 years (mean 26·3) to a total of 12 g. in 9 hours and its effect on the acid–base equilibrium observed. The respiratory volume was measured and the serum *p*H, total carbon-dioxide content of the blood, and packed erythrocyte volume estimated before, and at 2-hourly intervals after, administration of the aspirin over a period of 16 hours and again at the 28th hour. The carbon-dioxide tension of the blood and the bicarbonate concentration of the serum were calculated and the results at each 2-hour interval expressed as the mean value for the group as a whole. There was an average rise of serum salicylate to 39 mg. per 100 ml. after 10 hours, and 8 of the 10 subjects complained of symptoms of salicylism. The maximum displacement of the acid–base equilibrium occurred 2 to 4 hours after the maximum blood salicylate level was reached, the changes consisting of a fall in the carbon-dioxide tension of the blood of 11 mm. Hg, a rise in the serum *p*H of 0·06, and a fall in the serum bicarbonate concentration of 2·8 mM. per litre. At the same time, although the respiratory rate remained relatively constant, the respiratory volume increased by an average of 4 litres per minute (resting mean value 7·1).

The authors conclude that aspirin in therapeutic doses may result in a primary respiratory alkalosis due to hyperventilation without tachypnoea, and that the administration of alkalis to combat salicylism should not be undertaken without first estimating the blood carbon-dioxide content and *p*H. *D. I. Crowther*

2693. **The Effectiveness and Toxicity of Methadon, a New Analgesic Agent**
R. C. BATTERMAN and A. M. OSHLAG. *Anesthesiology* [*Anesthesiology*] **10**, 214–222, March, 1949. 21 refs.

This investigation into the effectiveness and toxicity of " methadon " (" amidone ") was carried out on 150 patients in hospital and 30 out-patients between the ages of 19 and 87 years. The drug was given both parenterally and by mouth. When given orally in doses of 5 mg. analgesia was not very satisfactory, and the incidence of toxic symptoms was high when administration was prolonged in patients with persistent pain. Parenteral administration of 10 mg. gave satisfactory analgesia in approximately 88% of the patients, and toxic reactions were less frequent; but mental confusion and toxic psychoses occurred in a large proportion of patients over the age of 50 who received the drug repeatedly for 5 days or more, regardless of the route of administration. Because of these untoward reactions it is concluded that methadon is not a satisfactory analgesic.
A. M. Hutton

2694. **The Pharmacology of the Optical Isomers of Amidone (2-Dimethylamino-4 : 4-diphenylheptan-5-one)**
R. H. THORP. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **4**, 98–114, March, 1949. 3 figs., 12 refs.

The analgesic potency, relative to that of a standard dose of morphine, of the D-, L-, and DL- isomers of " amidone " was determined in rats by a radiant-heat method; analgesic action was found to be associated only with the L-form which had about twice the potency of morphine. Acute intravenous toxicity in mice was equal for all three forms: LD 50 was 24 to 30 mg. per kg. Experiments with the isolated perfused heart of the rabbit showed that all the isomers are toxic to heart muscle and

cause death by this means. Relaxation of the rabbit ileum, thrown into spasm by carbamylcholine or barium chloride, was effected equally by all three isomers. In dogs and cats the fall in blood pressure caused by a first injection is very much less or absent after a second one. All three isomers have a local anaesthetic action, which is greatest with the L-isomer. *V. J. Woolley*

2695. **Antagonists for Fatal and Non-fatal Doses of Quinine Intravenously in Depressed Circulatory States and in Hyperthermia**

R. H. DREISBACH. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **95**, 347–351, March, 1949. 2 refs.

The author studied the toxicity of quinine, and the value of certain antagonists of its circulatory depressant effect, in haemorrhage, asphyxia of various degrees, hyperthermia, and shock.

The experimental work was carried out in rabbits and cats under pentobarbitone sodium anaesthesia. Haemorrhagic shock was caused by bleeding from the right femoral artery; asphyxia by allowing the animal to breathe through a rubber tube or by partly clamping the trachea; shock by opening the abdominal cavity and manipulating the contents; hyperthermia (41 to 42° C.) by the use of electrically heated pads. Quinine hydrochloride was injected intravenously after the fatal dose had been determined by continuous injection of a 1% solution in normal saline, given at the rate of 2 mg. per kg. per minute. The antagonists examined were adrenaline (epinephrine), neosynephrine, and calcium chloride, given at the same time as the quinine.

The depressant effects of quinine were increased in haemorrhage, severe asphyxia, hyperthermia, and shock. For example, in normal rabbits the median fatal dose of quinine was 208 mg. per kg.; after haemorrhage it was 146 mg. per kg. Adrenaline constantly antagonized the depressant effects of quinine in rabbits after haemorrhage and in shock and hyperthermia; in cats after haemorrhage and hyperthermia. It was not effective in reducing the fatal dose of quinine in asphyxia in either rabbits or cats. The other drugs were not consistently effective.

The author points out that in severe clinical malaria abnormal states similar to those studied, such as hyperthermia, may exist. It is possible therefore that the toxic effects of quinine may be enhanced in malaria. Quinine should therefore be used intravenously with caution and adrenaline as an antagonist should be given concurrently. [Intravenous administration of quinine is a satisfactory and safe therapeutic measure in careful hands, even when employed for the severely shocked patient. The author's views are, however, worth consideration.]

B. G. Maegraith

2696. **Action of Histamine on the Vascular System of the Rabbit Studied by Means of Radioactive Sodium.** (Actions de l'histamine sur le système vasculaire du lapin étudiées au moyen du radiosodium)

F. MOREL and M. MAROIS. *Comptes Rendus des Séances de la Socété de Biologie* [*C.R. Soc. Biol., Paris*] **143**, 464–468, April, 1949. 1 fig., 9 refs.

2697. **Actions of Sodium Azide**

J. D. P. GRAHAM. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **4**, 1–6, March, 1949. 7 figs., 24 refs.

The effects of administration of sodium azide, a neutral stable salt of hydrazoic acid, were studied by the author in various animals.

The LD 50 of the drug was determined in groups of white mice to be 28 to 34 mg. per kg. body weight by intraperitoneal injection, 19 mg. intravenously, and 27 mg. per kg. by mouth. Small doses of sodium azide (0·5 to 15 μg. per kg. body weight) caused a sharp transient fall in arterial blood pressure in cats and rabbits, probably resulting from a direct action on the smooth muscle of the blood vessels. This occurred also in anaesthetized eviscerated animals after atropine and vagotomy, after administration of " benadryl ", and after excision of the carotid sinuses and adrenalectomy; also in spinal cats similarly prepared. The effect was not modified by previous injection of eserine or nicotine. Volume recordings of the spleen and foreleg showed a decrease with the fall in pressure, but in 3 out of 10 preparations the spleen dilated actively. Perfusion of the hind limbs of the rat through the aorta with saline and measurement of the volume of the venous effluent showed that azide increased the rate of flow as a result of vasodilatation. Increasing the dose from 10 to 20 μg. per kg. body weight caused a rise in blood pressure in most animals. This was not modified by excision of the carotid sinus area or vagotomy, but was abolished by previous excision of the adrenals or by blocking agents such as " dibenamine " and dihydroergotamine. Since the effect could not be repeated after bilateral splanchnic nerve section, it is concluded that it was due to indirect stimulation of the adrenals through a sympathetico-adrenal mechanism. The injection of 50 μg. to 1 mg. of sodium azide into the inflow of the perfused heart of the cat increased the force of contraction, but not the rate, by direct stimulatory action on cardiac muscle, while 2 to 5 mg. caused a transient inhibition. Coronary flow increased owing to the action of the azide on the vessels. The injection of 10 to 100 μg. intravenously into anaesthetized cats and rabbits produced varying effects on the heart. Sometimes the rate and force of contraction increased, but in the majority of animals the heart was temporarily slowed. Atropine or vagotomy abolished this slowing, but left the increased force unaffected. Larger doses (5 to 10 mg. per kg. body weight) produced a marked initial slowing and inhibition of the heart followed by increase in cardiac activity above the initial level. The slowing was abolished by vagotomy or atropine and was therefore considered to be due to vagal inhibition. The increase in rate and force of contraction of the heart was not affected by giving dibenamine, but was prevented by previous adrenalectomy and was probably caused by the release of adrenaline. The resultant effect of these opposing actions on the circulatory system, as shown by variation in the spleen volume, was determined also by a number of other factors, such as the species of animal, its initial blood pressure, the sensitivity of its nervous system, the

anaesthetic, and the dose and rate of administration of the drug.

As a result of stimulation of the medulla the rate and depth of respiration was increased by sodium azide, which also dilated the bronchi by direct action on the smooth muscle. It also increased the activity of the gut and bladder, but had little effect on the uterus. Its stimulatory action on the central nervous system when given in sublethal doses caused occasional convulsive seizures in all types of animal used. It did not cause methaemoglobinaemia *in vivo*, although this occurs *in vitro*. *Vera N. Warren*

2698. **A Pharmacologic Comparison of Hexaethyl Tetraphosphate (HETP) and Tetraethyl Pyrophosphate (TEPP) with Physostigmine, Neostigmine and DFP**
P. R. SALERNO and J. M. COON. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **95**, 240–255, Feb., 1949. 6 figs., 23 refs.

Various alkyl polyphosphate compounds inhibit cholinesterase and thus produce physiological responses resembling those due to excitation of parasympathetic nerves. Two of these—hexaethyl tetraphosphate and tetraethyl pyrophosphate—were compared pharmacologically with physostigmine, neostigmine, and di*iso*propylfluorophosphonate. They all showed the same properties during a variety of tests. It is concluded that some of the pharmacological responses observed must be due to a mechanism other than the inhibition of cholinesterase.

[For details of the tests the original paper should be consulted.] *F. Hawking*

2699. **Antihistamine Drugs as an Antidote to the Histamine-like Action of Curare Preparations.** (Antihistaminica som Antidot mod Curarepræparaters histaminlignende Virkning)
H. POULSEN. *Nordisk Medicin* [*Nord. Med.*] **41**, 627–632, April 8, 1949. 10 refs.

The author investigated the efficacy of antihistaminic preparations in eliminating the undesirable side-effects of curare in electric convulsion therapy (E.C.T.) and in surgical anaesthesia. Nine patients were given altogether 41 sessions of E.C.T. with curare but no atropine or antihistaminic drug; hypersecretion (oral and bronchial) was present on 36 occasions. Five patients had 22 sessions with curare and atropine; hypersecretion was present on 5 occasions and a fall in blood pressure twice. A series of 86 patients underwent 423 sessions and received curare, atropine, and an antihistaminic drug "when indicated"; 56 of the patients had no symptoms requiring the use of an antihistaminic preparation. The remainder were later treated prophylactically with 100 mg. "antistin" or 50 mg. "anthisan" (mepyramine maleate) in the light of their reactions to the first session. Antistin reduced the expected hypersecretion in 19 sessions (48%) and anthisan in 26 sessions (96%). Anthisan also appeared the more effective in reducing bronchospasm and preventing a fall in blood pressure.

The value of these drugs in conjunction with curare during surgical anaesthesia was demonstrated by recording the incidence of capillary oozing in 75 sessions of anaesthesia without antihistaminic preparations and 155 with them. Oozing occurred in 16% of the former, in 8% of cases in which antistin was given a few minutes before the curare, and in only 3% of those in which anthisan was given. *B. Nordin*

2700. **The Decarboxylation of β-3 : 4-Dihydroxyphenylserine (Noradrenaline Carboxylic Acid)**
H. BLASCHKO, P. HOLTON, and G. H. S. STANLEY. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **3**, 315–319, Dec., 1948. 4 figs., 12 refs.

β-3 : 4-Dihydrophenylserine or noradrenaline carboxylic acid is not decarboxylated by extracts of guinea-pig kidney nor by extracts of adrenal gland. It is decarboxylated, however, by the L-tyrosine decarboxylase of *Streptococcus faecalis*, and the equivalent amount of noradrenaline is formed, as indicated by assays on blood pressure of the cat; the identity of the product with noradrenaline has been further confirmed by assay on rat uterus. It is concluded that noradrenaline carboxylic acid is unlikely to be the precursor of adrenaline or of noradrenaline. *G. A. H. Buttle*

2701. **The Vasodepressor Action of Noradrenaline**
G. B. WEST. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **4**, 63–67, March, 1949. 5 figs., 21 refs.

In cats which had received 5 mg. of ergotoxine or 15 mg. of "dibenamine" per kg., injection of 250 μg. of noradrenaline caused a fall in blood pressure which was more prolonged than that caused by adrenaline and did not reach such a low level; this did not occur in rabbits. No definite explanation of the effect is put forward. It is not changed by antihistamine substances and differs from the depressor effect of adrenaline in being reversed temporarily by 7 mg. of pentobarbitone. It may be due to constriction of the pulmonary artery. *V. J. Woolley*

2702. **On the Pharmacology of Dihydroergotamine.** [In English]
G. R. DE VLEESCHHOUWER. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **78**, 461–473, March, 1949. 8 figs., 13 refs.

In dogs under morphine–chloralosane anaesthesia a "reversal" of the normal pressor action of adrenaline into a purely depressor response could usually be obtained by injecting dihydroergotamine methanesulphonate intravenously in a dose of 0·1 mg. per kg. The cardioaccelerator action of adrenaline was not affected by giving dihydroergotamine. The pressor actions of nicotine and arterenol (noradrenaline) were antagonized less strongly; those of ephedrine and pituitrin scarcely at all. When it was injected slowly, dihydroergotamine had little direct effect on the blood pressure or heart rate. However, in all the dogs it increased notably the cardiac

response to electrical stimulation of the peripheral end of the right vagus nerve. The respiratory movements were temporarily depressed by dihydroergotamine.

Doses of the compound sufficient to reverse the pressor action of adrenaline had no comparable effect upon the vasoconstrictor response to stimulation of the splanchnic nerves, either in intact or in adrenalectomized animals. There appears to be " a real and complete dissociation " between the adrenolytic and sympathicolytic effects of dihydroergotamine and like substances. *F. N. Fastier*

2703. **The Comparative Pharmacology of the N-Alkyl-1-(*p*-Hydroxyphenyl)-2-Aminoethanols.** [In English]
D. F. MARSH and D. A. HERRING. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **78**, 489–498, March, 1949. 4 figs., 18 refs.

Circulatory effects of 1-(*p*-hydroxyphenyl)-2-aminoethanol and its N-methyl (" sympatol "), N-ethyl, N-*iso*propyl, N-*n*-butyl, and N-*tert.*-butyl derivatives were studied in dogs anaesthetized with sodium barbitone, in non-anaesthetized dogs, and in man. The hydrochlorides of the first two bases were found to be predominantly, but only weakly, pressor in action when injected intravenously into dogs in doses of from 0·025 to 0·2 mg. per kg. The higher homologues were predominantly depressor in action, particularly the tertiary butyl derivative. Optical manometer records obtained by the method of Remington and Hamilton indicated that all these agents increase cardiac output. When tested on cat and rabbit hearts perfused by the Langendorff method at low pressures, all of them considerably increased coronary flow without much change in the rate and force of the contractions. Only the *iso*propyl and tertiary butyl derivatives had a noteworthy effect in man when administered orally. As the diastolic blood pressure fell, the pulse rate increased. The authors suggest that, since the depressor compounds are not particularly toxic in man and are active when given orally in adequate dosage, they may be useful clinically in conditions in which an augmented coronary flow or peripheral sympathetic vasodilatation is needed. *F. N. Fastier*

2704. **Effects of a Quaternary Amine Capable of Blocking Functions of the Autonomic Nervous System**
F. H. LONGINO, J. R. CHITTUM, and K. S. GRIMSON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N. Y.*] **70**, 467–475, March, 1949. 4 figs., 5 refs.

2 : 6-Dimethyl-diethyl piperidinium bromide was administered intravenously in doses of 0·5 to 20 mg. per kg. to dogs in order to study the effects on the pulse rate, blood pressure, and vasomotor reflexes, and the responses to adrenaline and neostigmine. The vasopressor action of adrenaline was not prevented although several vasomotor reflexes were. Cardiac rate and blood pressure were reduced, but neostigmine (0·05 to 0·10 mg. intravenously) reversed all these actions. In man, lowering of blood pressure was consistently produced by intravenous doses of 0·5 to 1·5 mg. per kg. Pressor responses to breath holding were blocked or reversed, although cardiac rate was not markedly affected.

Fluoroscopic and radiographic studies of the gastrointestinal tract of dogs and balloon studies of activity of the stomach and small intestine in man indicated that 2 : 6-dimethyl-diethyl piperidinium bromide (1 mg. per kg. intravenously) causes a reduction in tone of the stomach and small intestine and abolishes their motor activity. In man " urecholine " (0·05 to 0·1 mg. per kg. intramuscularly) caused a partial reversal of the effect on gastric motility. Gastric acidity was reduced by the drug and complete recovery never took place under one hour.

When larger doses were given (up to 2 mg. per kg. intravenously), a feeling of warmth was experienced, and dryness of mucous membranes, dilatation of pupils, and loss of accommodation were noted. Most of these changes persisted for 30 to 60 minutes after intravenous injection. The drug was only slightly effective by the oral route. It thus appears that this quaternary amine is very potent in blocking actions mediated by the sympathetic and parasympathetic systems. *G. B. West*

2705. **The Effect of N-Methylation on Certain Iminazolines**
C. W. GOWDEY. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **4**, 45–50, March, 1949. 7 figs., 12 refs.

The N-methyl derivatives of 2-(1′-naphthylmethyl) iminazoline, 2-(N-benzylanilinomethyl)iminazoline, and 2-(*p*-methoxybenzyl)iminazoline were examined and compared with the parent compounds. In the case of the first parent compound, powerful vasoconstriction occurs when it is perfused through the rabbit's ear or dog's leg; the methyl-substituted compound does not do this, but large doses cause a marked rise in blood pressure by a stimulating action on the adrenals, this pressor effect being abolished by nicotine. The second parent compound has a depressor action in the cat; the methyl derivative is pressor, probably by a nicotine-like action. Both depress the isolated cat heart. The third pair of compounds resemble the second pair in most respects. The methyl derivative of the first compound stimulates the guinea-pig ileum, but all the other compounds inhibit it. All the compounds have some curare-like action and hinder transmission through the superior cervical ganglion. *V. J. Woolley*

2706. **The Action of Antagonists of Acetylcholine on the Vessels of the Rabbit's Ear**
J. H. BURN and N. K. DUTTA. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **3**, 354–361, Dec., 1948. 9 figs., 21 refs.

The effects of procaine, " benadryl ", quinidine, and atropine in abolishing the reaction of the vessels of the rabbit's ear to adrenaline and to histamine were compared. Both adrenaline and histamine normally produce a constrictor response, but in 2 exceptional cases dilator responses were observed.

" Earlier work has shown that a group of substances which includes atropine, benadryl, pethidine (demerol),

procaine, and quinidine have the common property of antagonizing the action of acetylcholine. Experiments on the perfused vessels of the rabbit's ear have now shown that these substances will also inhibit the constrictor action of adrenaline and sympathetic stimulation. When the constrictor action of adrenaline is reversed by " priscol ", those substances which inhibit the action of acetylcholine also inhibit the vasodilation caused by adrenaline. These substances, when perfused through the vessels, exert an action like that of ergotoxine or priscol; they reverse the constrictor action of adrenaline. These substances can themselves exert a constrictor action on the vessels, and this constrictor action, like that of acetylcholine seen in the rabbit's ear vessels after 24 hours, is reversed under the influence of priscol. In occasional fresh preparations, the injection of adrenaline regularly causes vasodilation; though after several hours' perfusion with Locke's solution, the injection causes vasoconstriction. The constrictor action of histamine in the rabbit ear vessels is abolished by the substances which abolish that of adrenaline. Priscol does not reverse the action of histamine. In occasional fresh preparations histamine causes vasodilation. The view that adrenaline has a dilator action of its own is discussed. The similarity in the action of adrenaline and acetylcholine is emphasized. The evidence is considered to support the theory of drug action by competition, and to suggest the mechanism of adrenaline reversal ".

G. A. H. Buttle

2707. **A New Synthetic Anticoagulant: " Tromexan " (G. 11705).** (Un nouvel anticoagulant de synthèse: le Tromexan (G 11705)

R. DELLA SANTA. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **79**, 185–206, March 5, 1949. 7 figs., bibliography.

" Tromexan " is the ethyl ester of 4 : 4′-dioxycoumarinyl acetic acid. It is a white crystalline powder sparingly soluble in water—although more so than dicoumarol—and can exist in two forms, one of which has a melting point of 151–153° C. and the other 176–179° C. (uncorrected). It is active by mouth and is well tolerated. Its action on the blood prothrombin level (estimated by Jeanneret's modification of Quick's method) is apparent within 3 hours and by rapid elimination of the drug the return to a normal level is usually accomplished within 24 to 48 hours. This easy reversibility constitutes one of the advantages of this anticoagulant, reducing the risk of haemorrhagic complications. However, care should be taken in all cases of liver disease, in which the blood prothrombin level may be depressed to a much greater degree, with slower recovery.

The effect of tromexan on coagulation time was studied in 31 subjects and prolonged it in 84% of cases, but the prolongation was not proportional to the fall in blood prothrombin level; when the coagulation time was doubled it was often found that the prothrombin level was reduced to a critical point. Its effect on capillary resistance was studied in 33 patients by the suction method, a definite depression of capillary resistance of 14 to 6 cm. Hg being found after tromexan had been given. Some patients developed petechiae and haematomata. The retraction of blood clot was uninfluenced and there was no deleterious effect on the thrombocytes in 28 patients. There was no alteration in the appearance of the erythrocytes, and intravascular haemolysis was not observed. The uterine musculature was affected, and care should be taken to reduce the dose during the menstrual period, since an excessive flow may be produced. In hepatic dysfunction, the blood prothrombin level recovered much more slowly. After a single dose of 600 mg. of tromexan in normal subjects the blood prothrombin level first fell to 75% of the initial value in in 24 hours, followed by a recovery phase of prothrombogenesis after the elimination of the anticoagulant. In this latter phase a slight hyperprothrombinaemia might occur. In cases of hepatic dysfunction two types of prothrombinaemia curve were demonstrated: (*a*) in cases of infective hepatitis the blood prothrombin level after a single dose of 600 mg. of tromexan fell to 60% of normal and recovery took 4 days; (*b*) in cases of severe hepatic disease such as cirrhosis of the liver the curve was even more depressed (15% of normal). Tromexan did not have any effect on the blood sugar or blood cholesterol levels; there was a transient depression of the blood fibrogen content, but there was no effect on renal function and renal disease did not appear to constitute a contraindication to its use; in a patient with only one kidney the lowered blood prothrombin level after tromexan rose to normal within 48 hours of cessation of treatment.

Tromexan was given in the form of tablets of 300 mg. No gastric intolerance was observed and absorption occurred rapidly in the duodenum. The daily dose given by the author was 1,200 mg. for 2 to 4 days, with a subsequent daily maintenance dose of 300–450 mg., irrespective of the body weight. The blood prothrombin level was determined daily during the first week, but once the level was stabilized at about 20% of normal determinations were made only once or twice weekly. If laboratory facilities are not available for determinations of the blood prothrombin level, a lower dosage should be employed to allow a margin of safety, that recommended being 900 mg. daily for the first 2 days, 600 mg. for the 3rd and 4th days, and then a daily maintenance dose of about 300 mg. On account of the rapid elimination of the drug from the body it is also of importance to apportion the dosage evenly during the first 24 hours, usually at 6-hourly intervals, while frequent determinations of the blood prothrombin level are necessary not only to prevent dangerously low levels being reached, but also to ensure that sufficient lowering is obtained. Although values as low as 10% of the normal were reached without producing any haemorrhage, 7 mild and 3 more serious cases of haemorrhagic complication were recorded, one of which ended fatally.

Tromexan was used clinically in the treatment of 73 patients, aged 16 to 79 years, 66 of whom were treated in the Cantonal Hospital at Geneva. Out of 40 cases of thrombophlebitis classified as " medical ", improvement was reported in 31, and out of 13 surgical cases, 11 were improved. After two or three doses the patients them-

selves drew attention to the fact that the limb felt lighter and that the pain was less intense; this improvement was accompanied by a fall in the prothrombin level. None relapsed during treatment, but after treatment a recurrence of symptoms occurred in 2 cases. In 2 patients with thrombosis of the retinal vessels and 6 with arteriosclerosis little improvement was obtained. Advanced cachexia, severe toxic infective conditions, and hepatic disease were regarded as contraindications to the use of tromexan.

[This is an important paper in view of the potential value of anticoagulants in therapeutics. An extensive bibliography is given.] *R. Wien*

2708. **A Study of Histochemical Iron Using Tracer Methods**

K. M. ENDICOTT, T. GILLMAN, G. BRECHNER, A. T. NESS, F. A. CLARKE, and E. R. ADAMIK. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 414–421, March, 1949. 5 refs.

The absorption and distribution of single test meals containing radioactive iron (1·35 mc. of Fe^{59} and 3·1 mc. of Fe^{55} per g. of food at the start of the experiment) were studied in rats, guinea-pigs, and dogs by histochemical, radioautographic, and tracer techniques. The iron was given by stomach tube as ferrous ammonium sulphate in milk or water. The iron demonstrated histochemically in duodenal mucosa, mesenteric and cervical lymph nodes, liver, and spleen appeared not to be derived from the single test meal. It accumulated over a long period when there was a high intake of iron and behaved like storage iron. The radioactive iron crossed the duodenal epithelium rapidly, and in the dog was not carried by the thoracic duct but by the portal circulation, for none was found in the thoracic duct up to 6 hours after the meal. The granular, histochemically visible iron of the duodenum did not affect the amount of iron absorbed, as shown by maintenance of rats on diets of known and varying iron content. There was no evidence to indicate direct participation of the reticulo-endothelial system in the absorption and transport of absorbed iron. *J. Dawson*

2709. **The Antidiuretic Effect of 3-Hydroxy-cinchoninic Acid Derivatives**

E. K. MARSHALL and K. C. BLANCHARD. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **95**, 185–190, Feb., 1949. 3 figs., 26 refs.

The antidiuretic effect of ten cinchoninic acid derivatives was tested in female dogs accustomed to catheterization.

Water diuresis was produced by administration by mouth of 40 ml. of water per kg. body weight and the urine was collected every 15 minutes. After diuresis was established, a solution of the sodium salt of one of the compounds was injected intravenously and its effect on the diuresis noted. The compounds were injected first in a dose of 20 mg. per kg. body weight and, if effective, this dose was reduced. Creatinine clearance was determined. Only 2-methyl-3-hydroxy-cinchoninic acid and 2-phenyl-3-hydroxy-cinchoninic acid had any antidiuretic effect, and of these the phenyl derivative was the more potent. Clearance tests showed that the glomerular filtration rate was not appreciably changed during the inhibition of diuresis by the drug, except for a period immediately after injection probably due to a secondary, transient, vascular effect of the drug. The antidiuretic effect was therefore considered to be due to increased reabsorption of water by the tubules. The antidiuretic effect of the phenyl derivative has also been observed by the authors in one " neurohypophysectomized " dog and a definite reduction in the polyuria of diabetes insipidus has been achieved by its oral administration to several human patients.

Vera N. Warren

2710. **Diuretic and Antidiuretic Action of Pituitrin During Intravenous Injection of Isotonic Solutions.** (Action diurétique et antidiurétique de la pituitrine au cours d'injections intraveineuses de solutions isotoniques)

E. DE MUYLDER. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **78**, 237–252, Feb., 1949. 2 figs., 25 refs.

The effect of pituitrin upon diuresis provoked by the intravenous injection of isotonic solutions of either sodium chloride (9 g. per litre) or glucose (50 g. per litre) was studied in rabbits. The solution, previously boiled and filtered, was infused into a marginal ear vein of an unanaesthetized rabbit at a rate of 150 ml. per hour and the diuresis, blood volume, and tissue diffusion were followed [the methods used are not described]. The arterial pressure (in a carotid loop) and the glomerular filtration (estimated from clearance of inulin) were sometimes recorded.

In 6 rabbits, an average of 34 ml. of urine in 1 hour was obtained by infusing saline and of 52 ml. with glucose solution. If pituitrin was added to the infusion fluid (2 milliunits in 150 ml.), these figures were reduced to 9 ml. and 26 ml. respectively, the differences being statistically significant. A shorter-lasting effect was obtained if the pituitrin was injected as a single dose intravenously or intramuscularly 10 minutes before the infusion. If the dose of pituitrin added to the infusion was increased to 2 units per 150 ml., the diuretic response to either glucose or salt solution was increased to about 100 ml. per hour. Single injections of pituitrin (2u.) intramuscularly or intravenously before the infusion increased the urinary flow to a lesser extent. Whatever the mode of injection, the increase in blood volume was intensified by either dose of pituitrin. The blood pressure was decreased by about 40 mm. Hg by the large dose: this was ascribed to weakening of the heart owing to coronary constriction. From the inulin clearance tests it was concluded that while small doses of pituitrin augmented, large doses inhibited tubular reabsorption. The difference between the saline and glucose diureses was ascribed to Verney's mechanism. [Investigation of the actions of intermediate doses of pituitrin would be interesting: perhaps one could be found which would have no effect on diuresis.]. *John R. Vane*

CHEMOTHERAPY

2711. **The Mode of Action of Salicylic Acid and *p*-Aminosalicylic Acid in Inhibiting the Growth of Tubercle Bacilli.** (Recherches sur le mode d'action de l'acide salicylique et de l'acide *p*-aminosalicylique dans l'inhibition de la croissance du bacille tuberculeux)
A. LUTZ. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **76**, 150–167, Feb., 1949. 4 figs., 34 refs.

A culture of *Mycobacterium tuberculosis* (bovine strain Vallée) was transferred in pieces of surface growth 5–6 mm. in diameter, after 8 days growth, to 50 ml. of the following medium in 200 ml. Erlenmeyer flasks:

Sodium dihydrogen phosphate, H_2O ..	3·0 g.
Potassium dihydrogen phosphate ..	4·0 g.
Magnesium sulphate, $7H_2O$	2·5 g.
Trisodium citrate, 5·5 H_2O	2·5 g.
Ferrous ammonium citrate, $12H_2O$ ..	0·01 g.
Asparagine, H_2O	5·0 g.
Glycerol	25·0 g.
Distilled water to	1 litre
(final *p*H 5·6).	

After convenient periods of growth at 37° C. the flasks were autoclaved at 120° C. for 45 minutes, the organisms filtered off on to weighed paper, washed five times with distilled water, dried for 16 hours at 70° C., and weighed.

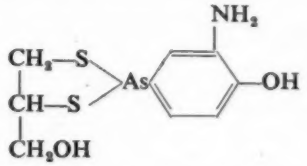
Addition of sodium pantothenate to this medium (20 mg. in 50 ml.) increased the rate of growth of *M. tuberculosis* in it, the mass of organisms recovered after 10 days growth being double that recovered from the medium alone, but by the 14th day of growth there was little difference. Sodium pantothenate partially reversed the inhibitory effect of salicylic acid on the growth of *M. tuberculosis*; it shortened the latent period produced by salicylic acid, but did not abolish it completely. Pantolactone had a similar effect; β-alanine no effect at all. Aneurin did not increase the effect of pantothenate or pantolactone, nor did sodium *p*-aminobenzoate. No anti-salicylic acid effect could be observed with aneurin, nicotinamide, pyridoxine, pyridoxal, folic acid, 2-methyl-1:4-naphthydroquinone, biotin, adenine, or guanine. Although *p*-aminobenzoic acid added to the basic medium did not increase the growth rate of *M. tuberculosis* it reversed the action of *p*-aminosalicylic acid. A similar but incomplete reversal was obtained by adding sodium pantothenate, while mixtures of pantothenate and *p*-aminobenzoate had an even greater effect. Biotin had a slight reversing effect on the inhibitory activity of *p*-aminosalicylic acid, but this might be due to some independent effect on growth. No anti-*p*-aminosalicylic acid effect was observed with folic acid, lactoflavine, nicotinamide, 2-methyl-1:4-naphthydroquinone, adenine or guanine.

On the basis of these experiments it is claimed that the reversal of the inhibitory effect of *p*-aminosalicylic acid on the growth of *M. tuberculosis* by *p*-aminobenzoic acid is non-specific, as the inhibitory effect is reversed by pantothenic acid and pantolactone.

C. L. Oakley

2712. **Condensation of 2,3-Dimercaptopropanol (BAL) with Oxophenarsine Hydrochloride: Toxicity and Chemotherapeutic Effect**
J. L. SAWYERS, B. BURROWS, and T. H. MAREN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 194–197, Feb., 1949. 1 fig., 12 refs.

The authors, working in the Department of Pharmacology and Experimental Therapeutics of the Johns Hopkins University, have described the preparation of the thioarsenite compound formed by condensing BAL with oxophenarsine to form BAL-OXO :



In the present paper they describe a comparison, as regards their toxicity and therapeutic value in mice infected with *Trypanosoma equiperdum*, of BAL-OXO with the parent oxophenarsine hydrochloride. Doses of both compounds were expressed as mg. of arsenic per kg. body weight. In experiments on toxicity all mice and rats were observed for 14 days. With oxophenarsine hydrochloride death occurred within 48 hours, but with BAL-OXO death was often delayed up to 96 hours. In therapeutic tests the mice were observed for 30 days; most animals died within the first 2 weeks, but 10 untreated controls died within 5 days. The acute toxicity of BAL-OXO was about one-quarter that of the oxophenarsine hydrochloride itself; these results differ radically from those of Peters and Stocken (*Biochem. J.*, 1947, **41**, 53) who found it to be about 4 times as toxic. The BAL-OXO compound has a much smaller therapeutic index (LD 50/CD 50=10) in mouse trypanosomiasis than has oxophenarsine hydrochloride itself (LD 50/CD 50=26 to 30). *Malcolm Woodbine*

See also Sections Radiology, Abstract 2760; Disorders of the Blood, Abstract 2874; Infectious Diseases, Abstracts 3049, 3070 (*a*) and (*b*), 3072.

STREPTOMYCIN

2713. **Streptomycin in Non-tuberculous Infections**
P. H. BUXTON, R. D. SIMON, and F. R. SELBIE. *Lancet* [*Lancet*] **1**, 729–733, April 30, 1949. 5 refs.

Streptomycin was given in 67 cases, consisting of: (1) 44 cases of urinary infection, chiefly by *Pseudomonas aeruginosa* and *Bacterium coli*; (2) 14 cases of wound infection, mainly by *Staphylococcus pyogenes*; (3) 9 miscellaneous infections. The infecting organisms were proved to be sensitive *in vitro* to streptomycin, but insensitive to the sulphonamides and to penicillin. The dose used in urinary infections was 3 g. daily for 4 days, usually given by intramuscular injection every 3 hours; potassium citrate was also given to keep the urine

alkaline. If there was much pain at the site of injection procaine was administered. For wound infections 4 g. was usually given daily for 2 days to obtain rapidly a high concentration in the tissues. Streptomycin was also injected subconjunctivally in cases of panophthalmitis, while surface infection was treated by the local insufflation of a powder containing streptomycin 1 g., penicillin 45,000 units, and sulphathiazole 9 g. Of the 44 cases of urinary infection, including 10 cases with suprapubic drainage and 9 cases after prostatectomy, 14 were cured and 12 improved. The criteria of cure were sterile urine and absence of symptoms of infection. In the cases in which suprapubic drainage was established there was a high proportion of failures due to reinfection. No advantage was gained by continuing treatment longer than 4 days, since the sensitivity of the organisms to streptomycin was then greatly reduced. Of the 14 cases of wound infection 10 were cured and 2 improved. Among the miscellaneous cases, staphylococcal infections resistant to other forms of chemotherapy responded well.

It is suggested that, if no improvement occurs within a week, surgical treatment should be considered with a view to eliminating inaccessible foci of infection and providing adequate drainage. Reactions were encountered in less than one-third of cases. No auditory symptoms were observed, but vestibular disturbance was pronounced in 3 cases. Less serious reactions included pain at the site of injection, headache, and nausea in about 10 to 20% of the cases. *R. Wien*

2714. **The Effect of Streptomycin, *para*-Aminosalicylic Acid (PAS) and Their Combination on the Tubercle Bacillus *in vitro* and *in vivo***
R. G. Bloch, K. Vennesland, and R. H. Ebert, and G. Gomori. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **59**, 554–561, May, 1949. 4 figs., 10 refs.

2715. **Ocular Complications of Intrathecal Streptomycin Therapy.** (Sur les accidents oculaires de la streptomycinothérapie intrarachidienne)
R. Weismann-Netter, J. Gandon, and H. du Sorbier. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **65**, 761–766, 1949.

2716. **Isolation of a Streptomycin-resistant Organism Capable of Utilizing Streptomycin for Growth**
G. L. Hobby and N. Dougherty. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **69**, 544–548, Dec., 1948. 2 figs., 4 refs.

A Gram-negative bacillus, the cultural properties of which did not permit of its assignment to any particular species, was isolated from an aqueous solution containing streptomycin sulphate in a concentration equivalent to 0·375 g. of pure base per ml. Growth curves showed that rapid profuse growth occurred at 37° C. and 22° C. in broth containing up to 0·5 g. streptomycin per ml. Somewhat slower growth occurred when the washed organisms were inoculated into an aqueous solution of 0·33 g. streptomycin per ml., although the total number of organisms after 24 hours' growth was the same as in the broth solutions. Scanty growth occurred in distilled water alone. Analysis of the sterile distilled water used throughout revealed the presence of less than 10 parts per million of solids. The authors consider this organism to be an example of a further category of streptomycin-resistant organisms. *J. E. M. Whitehead*

See also Sections Paediatrics, Abstract 2811; Respiratory Disorders, Abstract 2880; Infectious Diseases, Abstracts 3052–3.

OTHER CHEMOTHERAPEUTIC AGENTS

2717. **Experimental Studies on the Influence of Garlic Upon Cholera Vibrios.** [In English]
M. Popov. *Comptes Rendus de l'Académie Bulgare des Sciences* [*C.R. Acad. bulgr. Sci.*] **2**, 53–56, Jan.–March, 1949.

During the cholera epidemic in Bulgaria in 1912–13 garlic was thought to be of considerable value, thus confirming an old folk belief in the Balkans. Among Turkish troops [who presumably were so unenlightened as not to take garlic] the mortality from cholera was more than 50%; among Bulgarian troops it was 18%. Extracts of garlic or exposure of agar plates to the volatile oil of garlic inhibited growth of cholera vibrios. The antibacterial agent can be adsorbed by medicinal charcoal. *G. M. Findlay*

2718. **Assay of Aureomycin in Body Fluids: Observations on Individuals Receiving Aureomycin**
H. D. Brainferd, H. B. Bruyn, G. Meiklejohn, and M. Scaparone. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 318–321, Feb., 1949. 2 figs., 5 refs.

The authors, working at the San Francisco Hospital, have developed an assay method for aureomycin applicable to clinical studies of the antibiotic.

As test organism they employed an indigenous laboratory strain of a β-haemolytic streptococcus sensitive to 0·0039 unit of penicillin per ml. and 0·015 μg. of streptomycin per ml. The inoculum of 4,000 organisms per 0·5 ml. was obtained by diluting a 24-hour culture in brain-heart infusion broth after centrifuging with a special buffer broth used for the assay medium. The fluids for assay were stored at −40° C. until required and were Seitz-filtered before use unless already sterile. Serial two-fold dilutions were made in 0·2 ml. buffer broth, and 0·5 ml. of inoculum was added to give a final volume of 0·7 ml. The tubes were read after 18 hours' incubation at 37° C. As a control the organism was tested with known concentrations of aureomycin from a standard solution containing 10 μg. per ml.; the test organism was usually inhibited at 0·031 μg. per ml.

Some 30 individuals received aureomycin in doses varying from 0·16 to 2·5 g. orally, 50 to 100 mg. intravenously and 50 to 200 mg. intramuscularly. After peroral administration, the drug was present in the blood after 1 hour and its concentration reached a maximum after 2 to 4 hours. The peak concentrations

lay between 0·6 and 2·5 μg. per ml. of serum and measurable amounts persisted for over 6 hours. Intravenously, 50 mg. doses gave serum concentrations equal to or greater than those with 1 g. orally. Intramuscularly, 50 to 200 mg. doses, administered in a phosphate buffer with 2% procaine, led to a concentration greater than 0·15 μg. per ml. in only one case. In urine the concentration of aureomycin varied between 5 and 50 μg. per ml. depending upon the route of administration and the time of collection. *Malcolm Woodbine*

2719. **Aureomycin in Typhus and Brucellosis**
V. KNIGHT, F. RUIZ-SANCHEZ, A. RUIZ-SANCHEZ, and W. MCDERMOTT. *American Journal of Medicine* [*Amer. J. Med.*] **6**, 407–416, April, 1949. 3 figs., 12 refs.

To 11 patients with murine typhus, in whom the diagnosis had been confirmed by an increase in Weil–Felix titre, 4 to 6 g. of aureomycin was given by mouth daily in divided doses, starting on or before the 8th day in 8 cases, and on the 10th, 12th, and 16th days respectively in the remainder. The clinical condition of the patients improved within 24 hours, the headache and gastro-intestinal symptoms disappearing overnight and fever in 24 to 72 hours. One patient who was afebrile, however, showed no signs of improvement.

Five young adults with brucellosis were treated by the same regimen. Four of them had been febrile for 9, 26, 60, and 95 days respectively, and the fifth was afebrile. Bacteriaemia was present in 2 of the patients (one probably being infected with *Brucella melitensis*) and had previously occurred in the afebrile case. In all patients agglutinins for *Br. abortus* in titres varying from 1 in 80 to 1 in 640 were present in the serum. After treatment was started the temperature in the febrile cases fell to normal within 4 days and the clinical signs and symptoms rapidly disappeared. Febrile relapses occurred in 2 patients 14 and 42 days respectively after a course of aureomycin lasting for one week; this indicates that longer periods of therapy may be advisable.

As an addendum the authors quote 8 further cases of typhus treated in this way; rapid improvement took place in all. *R. Hare*

2720. **Neomycin, a New Antibiotic Active against Streptomycin-resistant Bacteria, including Tuberculosis Organisms**
S. A. WAKSMAN and H. A. LECHEVALIER. *Science* [*Science*] **109**, 305–307, March 25, 1949. 10 refs.

A preliminary account is given of " neomycin ", a new antibiotic active against mycobacteria. The organism producing neomycin, like that producing streptomycin, is a species of *Streptomyces* isolated from the soil and is related to *Streptomyces fradiae* isolated in 1915 by Waksman and Curtis. Neomycin is produced on both stationary and submerged culture of the organism in various media containing a source of nitrogen (peptone, meat extract), a carbohydrate (glucose), and sodium chloride. Extraction of the antibiotic from the medium, and its concentration, are carried out by adsorption-elution methods similar to those used for streptomycin.

Neomycin is a basic compound, most active at alkaline reactions; it is soluble in water, insoluble in organic solvents, and is thermostable. It is bacteriostatic against numerous Gram-positive and Gram-negative bacteria, including *Mycobacterium phlei* and *M. tuberculosis*, the antibiotic spectrum of crude preparations being distinct from those of streptomycin and streptothricin. Moreover, the drug is equally active against streptomycin-sensitive and streptomycin-resistant strains of *M. tuberculosis* (H37 Rv) and of *Bacterium coli* and does not permit growth of streptomycin independent strains of the latter. Neomycin is also highly bactericidal. Such preparations as are now in use are stated to have little or no toxicity to animals, and to protect them against experimental infection by various bacteria, including *Staphylococcus aureus* and *Salmonella* [but have apparently not yet been employed against tuberculous infection]. Resistance to neomycin has not been found among the organisms sensitive to it, nor has more than a limited degree of resistance developed after prolonged incubation of such organisms in contact with the drug. The antibiotic has not yet been obtained in crystalline form, but preliminary chemical studies suggest a distinct difference from streptomycin and streptothricin. *P. D'Arcy Hart*

See also Section Infectious Diseases, Abstract 3034.

2721. **The Enhancement of the Chemotherapeutic Action of Penicillin**
G. L. HOBBY, T. F. LENERT, W. REED, and D. RINNE. *Journal of Bacteriology* [*J. Bact.*] **57**, 247–252, Feb., 1949. 2 refs.

In experiments on mice infected with the author's strain of *Streptoccus pyogenes* it was found that certain degradation products of penicillin slightly enhanced the action of crystalline penicillin G and of highly purified penicillin dihydro-F. *G. Payling Wright*

See also Section Paediatrics, Abstract 2808.

2722. **Lack of Effect of Sodium Phenosulfazole (Darvisul) on Certain Experimental Virus Infections**
G. A. LOGRIPPO, D. P. EARLE, B. B. BRODIE, I. P. GRAEF, R. L. BOWMAN, and R. WARD. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 528–529, March, 1949. 2 refs.

2723. **Failure of Phenosulfazole (Darvisul) in Treating Experimental Viral Infections**
H. R. COX, H. KOPROWSKI, A. W. MOYER, G. R. SHARPLESS, and S. C. WONG. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 530–534, March, 1949. 7 refs.

2724. **Therapeutic Failure of Phenosulfazole (Darvisul) in Mice Infected with EMC or with MM Viruses**
M. L. WEIL and J. WARREN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 534–535, March, 1949. 2 refs.

TOXICOLOGY

2725. **Preliminary Report on Clinical Trials of Antabuse**
R. G. BELL and H. W. SMITH. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **60**, 286–288, March, 1949. 5 refs.

The Danish drug " antabuse " (tetraethylthiuramid-sulphide) has been tested at the request of the Canadian Medical Association with a view to assessing its validity in the treatment of alcoholism. This report is mainly concerned with the symptoms produced when alcohol is taken after antabuse. Before giving the drug to their patients the authors tried the effects of antabuse on themselves. On drinking a small amount of alcohol after taking 0·5 g. of antabuse daily for 4 days they experienced similar symptoms to those described by the Danish authors, such as sensation of heat in the face, unpleasant flushing, redness of the skin, and irritation in the throat with subjective dyspnoea. One of them experienced peripheral vascular collapse much more pronounced than would be expected from the small dose of alcohol taken. The drug was then tried on 9 alcoholic patients. It was found that the intensity and duration of the symptoms depended on the dose of alcohol taken and on the level of alcohol in the blood. In one man, who was a heavy drinker, 5 oz. (142 ml.) of whisky, taken over a period of one hour, produced severe signs of intoxication and cessation of breathing, which was eventually restored by artificial respiration and oxygen administration. The patient then vomited repeatedly for the next 4½ hours.

The authors warn against giving antabuse as a " sobering-up " drug; it should be withheld until it is known that the patient is free from alcohol. At present antabuse should be used only in carefully selected cases with a full realization of its potential dangers.

J. T. Leyberg

2726. **A Case of Thallium Poisoning.** (Przypadek zatrucia talem)
M. SZAJNA. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **4**, 369–370, March 21, 1949.

Nutritional changes in the lower limbs, baldness, " tearing " pains, and paraesthesiae suggest the possibility of thallium poisoning. In both the cases described the source of thallium was a rat poison. The author suggests that because of the increasing use of thallium poisons for killing rats the number of mildly poisoned persons may be considerable, especially since the characteristic baldness is preceded by the symptoms of polyneuritis. *J. H. Czekalowski*

2727. **The Treatment of Methanol Poisoning with Ethanol, with Report of Two Cases**
K. AGNER, O. HÖÖK, and B. VON PORAT. *Quarterly Journal of Studies on Alcohol* [*Quart. J. Stud. Alcohol*] **9**, 515–522, March, 1949. 2 figs., 12 refs.

The oxidation of methanol (methyl alcohol) by alcohol dehydrogenase is inhibited by the presence of ethanol, since both compete for oxygen. Reducing the rate of methanol oxidation will delay the production and excretion of toxic products and of acidosis, and thus alleviate the symptoms. The authors describe two cases of methanol poisoning, one in a chronic alcoholic aged 41 working at a factory in which methanol was used, the other in a friend whom he invited to drink a glass of " brandy ", that is, methanol. The former lost consciousness the next morning after complaining that he could see nothing. He was cold and sweating, his reflexes were absent and pulse rate and blood pressure raised. Large amounts of methanol were found in the blood, and the alkali reserve was low. In an attempt to raise this, large amounts of 5% bicarbonate solution were given intravenously, together with 70 ml. of ethanol in 1,000 ml. of 1·3% bicarbonate; he was also given penicillin, but he died of pneumonia 24 hours after admission. In the second, symptoms of methanol poisoning—apathy, blurred vision, and slow speech—developed more slowly, and were milder. He was given, by mouth, a total of 120 ml. of ethanol over a period of about 3 days, whenever the symptoms started to appear. Methanol concentration in blood and alkali reserve were determined by repeated analyses. He left hospital free of symptoms. In both cases the ethanol had the effect of delaying the excretion of methanol. *T. E. C. Early*

2728. **The Toxicity of Vesicants and Some Other Compounds to the Pyruvate Oxidase System (Brain)**
R. A. PETERS and R. W. WAKELIN. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **4**, 51–62, March, 1949. 1 fig., 41 refs.

Oxygen uptake of pigeon brain tissue in the presence of pyruvate and various toxic vesicants was determined. Dichlorodiethyl sulphone and divinyl sulphone were the most toxic of the substances tested and, in most of them, the inhibition of oxygen uptake was proportional to vesicant action. The only exception was divinyl sulphone, which was relatively less effective as a vesicant. These two substances are believed to act almost exclusively on sulphydryl groups; mustard gas is less toxic and its action is less specific, although all of them are believed to act on the pyruvate system. *V. J. Woolley*

2729. **Toxic and Pathologic Effects of Xylidine in the Fasting and Non-fasting States**
S. S. SPICER, B. HIGHMAN, and A. R. MONACO. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **95**, 256–261, Feb., 1949. 9 refs.

The effect of exposure to a xylidine-laden atmosphere on fasting cats and on cats after a high protein meal is described. The animals were exposed in a 400-litre chamber into which was passed a stream of air which had previously bubbled through pure xylidine at a rate of about 20·6 litres per minute, an additional air supply of 170 litres per minute ensuring adequate ventilation, and were kept under observation for about 16 hours. The fasting animals were given no food for 24 to 48 hours before exposure and the other animals were force-fed by gastric intubation with yeast and milk, with or without additional liver powder or meat. The xylidine concentra-

tion in the chamber was measured periodically and varied between 0·10 and 0·27 mg. per litre.

All the fasting animals survived longer than 24 hours, while 46% of the fed animals died during, or within 24 hours of, exposure. The fed cats reacted to xylidine with an acute disturbance characterized by hyperpnoea, salivation, and agitation. Death followed in some cases, but in those cats who survived several hours the symptoms began to subside despite continued exposure, indicating that susceptibility to xylidene poisoning is increased during food absorption. Survivors of both groups developed a high concentration of methaemoglobin and Heinz bodies in the blood, often followed by a severe haemolytic anaemia and jaundice. The hyperpnoea of the fed animals was not related to the high level of methaemoglobin in the blood, which did not develop until later. Metabolic derivatives of xylidine appeared to be excreted in the saliva of surviving animals. Histological studies were made on the tissues of cats of both groups. Pulmonary oedema was found chiefly in the hyperpnoeic animals. Haemosiderosis occurred in the spleen, liver, lungs, and renal tubules, and the liver showed necrotic lesions in animals of both groups. The kidneys and thymus were congested and the myocardium showed fatty degeneration.

Vera N. Warren

2730. **Morbid Anatomy of Tri*ortho*cresyl Phosphate Poisoning.** (Die pathologische Anatomie der Triorthokresylphosphatvergiftung)
B. WALTHARD. *Virchows Archiv für Pathologische Anatomie und Physiologie* [*Virchows Arch.*] **316**, 619–665, 1949. 23 figs., 27 refs.

2731. **Studies on the Toxicity and Pharmacological Action of *p*-Dimethylaminobenzenediazo Sodium Sulfonate (DAS)**
R. G. HERRMANN and K. P. DUBOIS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **95**, 262–271, Feb., 1949. 7 refs.

Measurement of the toxicity of *p*-dimethylaminobenzenediazo sodium sulphonate (DAS) administered intraperitoneally gave the following approximate LD 50 values in mg. per kg. body weight: albino rats 15, albino mice 70, guinea-pigs 30, rabbits 10 to 20, and dogs 5 to 10. The oral LD 50 for albino rats was about 55 mg. per kg. No tolerance to DAS was observed in rats and the rodenticide was acceptable and produced high mortality of rats when placed in the diet at concentrations of 0·5% and 1%. Toxicity measurements on N,N-dimethyl-*p*-phenylenediamine given intraperitoneally gave the following LD 50 values in mg. per kg.: albino rats 21, mice 25, guinea-pigs 45, rabbits 100, and dogs 10 to 20. The differences in species susceptibility to this compound and DAS suggest that the latter substance does not undergo cleavage at the azo linkage before exerting its toxic effect. DAS caused a generalized depression in all species, degeneration of the kidney tubules, hyperaemia of the intestine and liver, a fall in blood pressure, and respiratory paralysis. Hyperglycemia followed by hypoglycemia occurred in animals poisoned by DAS. The extent of these changes was dependent upon the dose of DAS and the species susceptibility to the agent. The hyperglycemia could be prevented by insulin or by adrenal-demedullation, but survival of the animals was not influenced by these treatments. The hypoglycemic convulsions could be terminated or prevented by glucose which prolonged the survival time but did not prevent ultimate death of the animals. A depletion of liver and muscle glycogen of rats was observed after administration of DAS and the animals were unable to deposit liver glycogen from injected glucose; this indicated that DAS exerts an inhibitory action on glycogen synthesis.—[Authors' summary.]

2732. **The Effect of *p*-Dimethylaminobenzenediazo Sodium Sulfonate (DAS) on the Enzymatic Reactions of Intermediary Carbohydrate Metabolism**
R. G. HERRMANN and K. P. DUBOIS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **95**, 272–284, Feb., 1949. 1 fig., 10 refs.

The effect of *p*-dimethylaminobenzenediazo sodium sulphonate (DAS) on intermediary carbohydrate metabolism in rat, mouse, and guinea-pig tissues was investigated *in vivo* and *in vitro*. The authors had previously found (see Abstract 2731) that owing to inhibition of glycogen synthesis the liver and muscle glycogen of DAS-poisoned rats was depleted. Incubation *in vitro* with DAS inhibited the succinic dehydrogenase activity of rat liver and kidney only after a lag period during which time it appeared that the compound had undergone a chemical change. Cleavage at the azo linkage would yield a diamine which may inhibit succinic dehydrogenase. However, no decrease in the succinic dehydrogenase activity of liver was observed when the livers were removed 5 hours after intraperitoneal administration of 30 mg. of DAS per kg. body weight *in vivo*. No inhibitory effect was observed on cytochrome oxidase, malic dehydrogenase, or fumerase, and DAS had no effect on the rate of anaerobic glycolysis of rat-brain homogenate and rat-liver slices. The oxidation of glucose by rat-brain homogenate was inhibited *in vitro* by concentrations of DAS above 1×10^{-6} M; no such inhibition was observed with brain tissue from rats poisoned with DAS *in vivo*. DAS had an inhibitory action on cellular respiration of liver tissue *in vitro* and *in vivo*.

The effect of DAS on the respiration of liver slices *in vitro* was tested with the following intermediates of the Krebs citric acid cycle as substrates: fumarate, malate, succinate, citrate, pyruvate, oxalacetate, and l-glutamate. It was found that the oxidation of malate, succinate, and oxalacetate was unaffected by addition of DAS, while the additional oxygen consumption due to fumarate, pyruvate, and citrate was decreased by the presence of 1×10^{-4} M DAS. The inhibition of the utilization of pyruvate and citrate also occurred when tested with livers of rats poisoned *in vivo* 5 hours previously with 30 mg. per kg. body weight of DAS. Finally, the livers and kidneys of rats poisoned with DAS were examined for phosphorylated intermediates of glycolysis, the most striking findings being the depletion of phosphocreatine and the marked increase in inorganic phosphorus. DAS

had no effect on the phosphocreatine content of the heart and skeletal muscle. Further experiments showed that DAS is a strong inhibitor of aerobic phosphorylation *in vitro* and *in vivo* and that this effect is not due to inhibition of oxygen consumption, but rather to a direct action on the transphosphorylating mechanism. There was a correlation between the species susceptibility to acute poisoning by DAS and the dose necessary to inhibit aerobic phosphorylation *in vivo*. *Vera N. Warren*

See also Section Physiology and Biochemistry, Abstract 2684.

INDUSTRIAL TOXICOLOGY

2733. Physiological Response of Man to Ammonia in Low Concentrations

L. SILVERMAN, J. L. WHITTENBERGER, and J. MULLER. *Journal of Industrial Hygiene and Toxicology* [*J. industr. Hyg.*] **31**, 74–78, March, 1949. 2 figs., 7 refs.

In the United States the accepted permissible limit for the inhalation of ammonia is 100 parts per million, but exposure to concentrations of 500 parts per million is said to be without ill effects. Seven adults inhaled air-ammonia mixtures containing 500 parts of ammonia per million of air. Subjective reactions varied, but were severe in 2 subjects, and included irritation of the nose and throat, hypoaesthesia of the exposed skin, and lacrimation. The respiratory volume and rate were markedly increased. Hyperventilation with rise in minute volume by 50 to 250% took place cyclically with decreases of 25% every 4 to 7 minutes. Ammonia retention decreased progressively until 80% of the inhaled ammonia was returned in the expired air. Exposure to 500 p.p.m. of ammonia is undesirable. *T. A. Lloyd Davies*

2734. Short-term Toxicity Tests on the Mono and Di Methyl Ethers of Hydroquinone

H. C. HODGE, J. H. STERNER, E. A. MAYNARD, and J. THOMAS. *Journal of Industrial Hygiene and Toxicology* [*J. industr. Hyg.*] **31**, 79–92, March, 1949. 10 figs., 4 refs.

The toxicity of the monomethyl (MME) and dimethyl (DME) ethers of hydroquinone (which have the property of absorbing ultraviolet light and may therefore be incorporated in sun-tan lotions) was tested in mice and rats by intraperitoneal and oral administration. In each species MME was three to five times more toxic than DME, the rat being considerably more susceptible. However, the acute toxicity of MME was only moderate, the LD 50 for intraperitoneal administration in the rat being of the order of 400 mg. per kg. body weight.

Adding MME to the diet in amounts of 0·1% for male rats and 0·5% for female rats for one month depressed growth. Adding 2% DME caused some slowing of growth (greater in male than in female rats). As these additions made the diet unpalatable, depression of growth may have been due to lessened intake of food. No significant changes were discovered at necropsy. Additions of 10% were needed to cause rabbits to lose weight. Dogs were able to tolerate large additions to the diet of MME and DME (up to 6 mg. daily). The application of concentrations of MME and DME up to 10% in a sun-tan lotion to the depilated skin of rabbits 5 days a week for 30 days produced no significant general effects, but there were unmistakable dryness and crusting of the skin. Microscopical examination showed inflammation and ulceration. Less severe changes were caused by the sun-tan lotion alone. Application of 10% solution of MME and DME for 3 hours, after which the solution was washed off, caused some erythema and thickening and cracking of the skin after 12 applications. The local effect of MME was greater than that of DME.

[The technique adopted to test skin irritation is important and worthy of more elaborate description than is given.] *T. A. Lloyd Davies*

2735. Vanadium Pentoxide Poisoning. (Förgiftning av vanadinsyra (V_2O_5))

S.-G. SJÖBERG. *Nordisk Medicin* [*Nord. Med.*] **41**, 500–503, March 18, 1949. 17 refs.

In December, 1946, the author was consulted by a 36-year-old worker employed in the production of vanadium pentoxide, who complained of irritation in the throat, wheezing in the chest, dry cough, and increasing fatigue. The 36 employees at this workshop were subsequently thoroughly investigated, with the result that a fairly clear-cut syndrome of vanadium poisoning was discovered. In its most extreme form this syndrome consisted of sore throat, dry cough, rhonchi in the chest, dyspnoea on exertion, palpitations, fatigue, and lethargy. Some workers had sore eyes or a papular rash on the extremities. There were 4 cases of bronchopneumonia, one case of lobar pneumonia, and one of pleurisy. The syndrome cleared up within a few weeks on removal of the patient from work, but returned soon after employment was resumed. None of the patients had the green discoloration of the tongue described by Wyers in British workers. In cases of eczema patch tests with sodium vanadate gave positive reactions. The author has performed some experiments on animals which showed that high concentrations of vanadium pentoxide cause rapid death of rabbits from pulmonary oedema or acute respiratory distress. Experiments are in progress to demonstrate the effect of low concentrations on animals over a long period. *B. Nordin*

2736. Alkyl Mercury Compound Poisoning: Clinical Aspect and Risks of Exposure. (Den kliniska bilden vid förgiftning med alkylkvicksilverföreningar samt expositionsrisker)

G. AHLBORG and A. AHLMARK. *Nordisk Medicin* [*Nord. Med.*] **41**, 503–504, March 18, 1949. 1 fig., 6 refs.

The authors describe a case of mercury poisoning in a farmer after a spring sowing of 1,500 kg. of mercury-steeped seed. A month after the sowing was complete, the farmer developed numbness in the fingertips and increasing motor ataxia. After 6 months, his speech became slurred and finally unintelligible, and on admission to hospital he was also found to have spinal automatism. His condition deteriorated, muscular atrophy developed, and he became unable to write or feed

himself. He had athetosis, a positive Babinski sign, patellar clonus, and laughing fits. The diagnosis of mercury poisoning was confirmed by the discovery in urine samples of 166 and 256 μg. of mercury per litre. He was treated with BAL (12 g. total dose) and this caused a sharp rise in the urinary excretion of mercury. He improved slowly after this treatment, until he could walk with assistance, feed himself, and write and speak intelligibly. *B. Nordin*

2737. **Absorption and Elimination of Carbon Disulfide in Man**

J. TEISINGER and B. SOUČEK. *Journal of Industrial Hygiene and Toxicology* [*J. industr. Hyg.*] **31**, 67–73, March, 1949. 2 figs., 5 refs.

Nine men, not previously in contact with carbon disulphide (CS_2), were exposed to the inhalation of air-vapour mixtures. The CS_2 in air and blood reached equilibrium in 2 hours at a level proportionate to exposure. During the first 15 minutes of exposure 80% of inhaled CS_2 was retained, but after 45 minutes and until the end of the experiments (up to 4 hours) this figure was reduced to a nearly constant level of 40%. Of the retained CS_2 excretion by the urine was slight (0·06%) and only 5% was eliminated through the lungs; 93 to 95% of retained CS_2 was metabolized. Examination of 12 workers in a viscose plant (previously exposed to CS_2 inhalation) revealed a much lower degree of retention which after the first 15 minutes decreased rapidly. Substantial quantities of CS_2 were eliminated in the urine.

T. A. Lloyd Davies

2738. **On the Theory and Pathology of Carbon Disulfide Poisoning. I. Effect of Carbon Disulfide on Tissue Respiration and Glycolysis. II. *In vitro* Effects of Carbon Disulfide on Blood Cells and Bone Marrow. IV. Effects of Carbon Disulfide on the Heart**

R. H. DEMEIO, H. BRIEGER, and M. H. F. FRIEDMAN. *Journal of Industrial Hygiene and Toxicology* [*J. industr. Hyg.*] **31**, 93–105, March, 1949. 4 figs., 29 refs.

Very low concentrations of carbon disulphide (CS_2) injure nerve tissue, so the effect of CS_2 cannot be interpreted as a solvent action. The authors' paper reports, without comment, the effect of CS_2 on respiration and glycolysis, enzyme activity, the blood and bone marrow, and the heart. Respiration was studied in tissue slices of rat brain, liver, and kidney and in tissues of rabbits exposed to inhalation or intravenous injection of CS_2; glycolysis in slices of rat brain, liver, and kidney and in diaphragm strips. Oxygen consumption was not inhibited in tissues of rabbits exposed to CS_2, and tissue-slice experiments gave unreliable results, but some indication of inhibition was obtained. Anaerobic glycolysis in the rat slices was decreased by 16 to 63% by 0·006 to 0·0095 M CS_2. Irregular variations in aerobic glycolysis were produced. No significant change in the *in vitro* activity of lipase, pepsin, and trypsin resulted from exposure to CS_2 liquid and vapour. Forty-eight 6-hour exposures of rabbits to 300 p.p.m. of CS_2 (concentration in blood $1·62 \pm 0·17$ mg. CS_2 per litre) were needed to produce slight diminution in reticulocyte count (within normal range), slight increase in erythrocyte resistance, and significant increase in pseudo-eosinophilic cells (corresponding to neutrophilia in man) and decrease in the number of lymphocytes. The myelocytic activity of the bone marrow was increased.

Intravenous injection of 0·5 ml. CS_2 killed rabbits within 20 minutes, the electrocardiogram showing typical signs of a dying heart. After exposure of rabbits to 1,100 p.p.m. of CS_2 for 6 hours on twelve occasions (mean concentration in blood after a single exposure $14·3 \pm 2·1$ mg. per litre) the electrocardiogram showed only minor changes. Histologically, only hyaline degeneration of individual muscle fibres was found. Similar results were obtained after 48 exposures to 300 p.p.m. for 6 hours (mean concentration in blood after a single exposure $1·62 \pm 0·17$ mg. per litre).

T. A. Lloyd Davies

2739. **Experimental Study of the Haematopoietic Action of Cobalt. III. Cytological and Histological Findings.** (Studio sperimentale sull'azione emopoietica del cobalto. III. Reperti cito- ed isto-patologici)

V. VALERIO. *Folia Medica* [*Folia med., Napoli*] **32**, 104–113, March, 1949. 9 figs.

The author gives his third report on the effects of cobalt on guinea-pigs. On macroscopical examination little difference was noted between the experimental and the control animals. The controls weighed slightly more; the tissues of the treated animals were somewhat more congested. Many organs were very engorged and subserous petechiae and even haemorrhages were seen in the adrenals. The bone marrow was very bright red and in a state of great activity in test animals. This increased activity was most marked in the red cell group and in the histio-reticulocytes. The erythroblasts tended to clump as though forming a syncytium; sometimes only one phase of maturation could be seen in the group, sometimes several. In these clumps histiocytes were often seen surrounded by erythroblasts. All the erythrocytes showed marked anisocytosis and the nuclear structure, often basophil, resembled that in histio-reticulocytes with nuclei of human megaloblastic type. In the less mature cells of the granuloblast series the nuclear structure was often of histio-reticulocyte pattern. Both in the erythroblast and granuloblast series the more mature forms predominated. Many giant cells were seen. Among histio-reticulocytes the author noted; (1) cells of haemohistoblast appearance; (2) true reticulo-histiocytes; (3) cells considered to be of mesenchymal type and differing structurally from those in the first two groups by an absence of granulation, by their greater size, and by the presence of a large and often irregular nucleus, which stained lightly and contained many nucleoli; (4) plasmocytes; (5) lympho-monocytes of uncertain nature; (6) large macrophages with irregular nuclei.

Histological sections showed a rich cellular element, notably of giant cells. Some megakaryocytes contained lymphocytes or eosinophils. Macrophages were noted with a yellow pigmentation. Various other organs were examined and the general picture was one of congestion,

reticulo-histiocyte activity with active formation of erythrocytes, and phagocytosis. Some degenerative and inflammatory changes were also observed.

It is thought that there was no evidence of extramedullary erythropoiesis. As some authors postulate a hepatic cirrhosis due to cobalt, future experiments will be directed to investigating this possibility. *G. C. Pether*

2740. **Comparative Toxicity of Methacrylonitrile and Acrylonitrile**
W. A. McOmie. *Journal of Industrial Hygiene and Toxicology* [*J. industr. Hyg.*] **31**, 113–116, March, 1949. 6 refs.

Methacrylonitrile and acrylonitrile are used in the manufacture of synthetic rubber. Vapour of both nitriles is very toxic to mice; with methacrylonitrile all mice, and with acrylonitrile 5 out of 6 mice, died after inhaling 5·8 mg. of vapour per litre of air for 30 minutes. None died after inhaling 0·6 mg. of either nitrile per litre for 30 minutes.

Acrylonitrile is less toxic to rats than to mice. Increased activity was the first sign that mice were affected, followed by hyperpnoea which continued until rapid shallow breathing occurred. This was followed by gasping, apnoea, and death. If the exposure stopped before rapid respiration developed the mice recovered, but otherwise death took place within 24 hours. Both nitriles were irritant when applied to the clipped skin of rabbits; methacrylonitrile has greater powers of penetration (one rabbit died after application of 2 ml. per kg. over 100 sq. cm. of shaved abdomen) but acrylonitrile is more irritant. One rabbit, moribund after the application of 4 ml. per kg. of methacrylonitrile to 200 sq. cm. of shaved abdomen, was saved by the intravenous injection of 20 mg. per kg. of sodium nitrite. One drop (0·05 ml.) of each nitrile caused acute conjunctivitis. Acrylonitrile seemed more irritant. Intragastric and intraperitoneal injection of the substances into mice showed methacrylonitrile to be slightly more toxic. The approximate intragastric lethal dose was 15 mg. per kg. for methacrylonitrile and 20 mg. per kg. for acrylonitrile, and the lethal intraperitoneal dose was 15 mg. per kg. for both nitriles. These doses are of the same order as the lethal doses of inorganic cyanides.

T. A. Lloyd Davies

2741. **The Problem of Acetone Toxicity. Results of our Experimental Studies on the Rabbit and Guinea-pig.** (Le problème de la toxicité de l'acétone. Résultats de nos recherches expérimentales chez le lapin et le cobaye) —. Dervillée, —. L'Épée, and —. Jaulin. *Archives des Maladies Professionnelles* [*Arch. Mal. prof.*] **10**, 125–129, 1949.

Having detailed some of the many uses of acetone in industry and noted the general opinion as to the harmlessness of this solvent, the authors quote 2 published cases of acetone poisoning and describe the results of experiments with guinea-pigs and rabbits. In air containing 0·592 g. of acetone vapour per litre, guinea-pigs survived for 2½ hours and rabbits for only 1½ hours. After a stage of anxiety and agitation with disturbance of equilibrium, accompanied by an intense catarrh of the eyes and nose and increasing difficulty in breathing, there followed a period of torpor which ended in death. A vasomotor disturbance was manifest in injection of the paws, muzzle, and ears. With a lower concentration of vapour, or a shorter period of exposure, death only occurred after repeated exposure. After non-lethal exposure, acetone and acetoacetic acid were excreted in the urine, the degree of acetonuria appearing to be proportional to the intensity of the intoxication. Neither albumin nor sugar was found in the urine. A slight leucocytosis with marked eosinophilia appeared in the guinea-pigs after about one week of repeated exposure and persisted throughout the experimental period, gradually diminishing after exposure had ceased; there was no significant alteration in the erythrocyte count or the haemoglobin content of the blood. These changes were seldom seen in the rabbit. There was a marked loss of weight, up to one-third of the original body weight being lost although no experiment continued for longer than 2 months.

The pathological changes were more marked in the animals which died after repeated exposure. The lungs were congested, with exudation into the alveoli and infiltration of their walls, desquamation of the bronchial epithelium, occasional atelectasis, and (in one case) sclerosis of the lung tissue. The liver, scarcely affected in acute poisoning, showed degenerative changes of a fatty nature after repeated exposure. The convoluted tubules and glomeruli of the kidneys were also affected and ulcers of varying size were found in the gastric mucosa in many cases. There was no sign of absorption through the skin.

It is concluded that although the irritative effect of acetone upon the upper respiratory passages is generally effective in preventing acute intoxication, there is a danger that the inhalation of repeated small doses may produce similar degenerative changes in the liver and kidneys and ulceration in the gastric mucosa in man. The same precautions should therefore be taken in using acetone as are employed in industry in respect of other toxic solvents. *M. A. Dobbin Crawford*

See also Section Radiology, Abstract, 2753

THERAPEUTICS

2742. **Blood Groups and Subgroups of the Newborn. I. The A Factor of the Newborn**
E. Witebsky and L. M. Engasser. *Journal of Immunology* [*J. Immunol.*] **61**, 171–178, Feb., 1949. 11 refs.

Sera from human adults immunized with human blood group A substance agglutinate adult erythrocytes of subgroups A_1 and A_2 and cord blood erythrocytes of group A to the same titre if saline is used as the diluent. If the immune serum is diluted with normal adult serum (group A or AB) instead of saline, it is possible by its use to differentiate between adult A_1 and A_2 erythrocytes. Cord erythrocytes of group A more often resemble adult erythrocytes of group A_2 than those of A_1.

If purified A substance is added to human immune anti-A sera, the neutralized serum will no longer agglutinate any group A erythrocytes (A_1 or A_2) if saline is used as diluent. If such neutralized sera are diluted in adult human serum of group A they frequently agglutinate A_1 erythrocytes to the original titre but fail to agglutinate A_2 erythrocytes. When tested with these reagents, the erythrocytes of 34 babies belonging to group A showed wide differences in agglutinability. About half reacted as adult A_2 erythrocytes do, or even more weakly; the others agglutinated at serum dilutions between those characteristic of adult A_2 and A_1 erythrocytes, rarely reaching titres typical of adult A_1 erythrocytes. These findings are advanced to support Hirzfeld's " pleiades " theory (1947). *C. L. Oakley*

2743. **Further Observations on Isosensitization to the Rh Factor**
A. S. WIENER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 576–578, April, 1949. 7 refs.

Rh_1 blood was injected intravenously into 47 Rh-negative subjects at intervals of 3 to 4 months. After each injection an increasing number—up to 78% after the sixth injection—had developed Rh antibodies. None of 19 Rh_1Rh_1 individuals developed antibodies after a similar number of injections of Rh-negative blood.
John F. Loutit

2744. **Severe Renal Failure after Administration of Apparently Compatible Blood**
A. C. BUCHAN and J. WALLACE. *British Medical Journal* [*Brit. med. J.*] **1**, 660–662, April 16, 1949. 16 refs.

A case of mismatched transfusion is described in which Rh-positive blood was given to a previously transfused Rh-negative man, with disastrous and almost fatal consequences. Hyperimmune Rh antibody was present in the patient's serum.

The authors stress the importance of determining the Rh group of patients previously transfused and the unreliability of simple compatibility tests by means of cells suspended in saline, since only simple agglutinins are detected in this way. *John Murray*

2745. **Transfusion of Leukocytes and Products of Disintegrated Leukocytes**
A. S. WEISBERGER, R. W. HEINLE, and R. HANNAH. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 749–753, April, 1949. 4 refs.

Rabbit leucocytes were obtained from the peritoneal cavity, into which saline had previously been injected. These cells, suspended in Tyrode solution, were transfused intravenously into the same rabbit or into other rabbits. From other preparations the leucocytes were disintegrated by supersonic vibration and the supernatant fluid was infused. In each case there was an immediate development of leucopenia followed some hours later, in the majority of instances, by leucocytosis. Control experiments with the infusion of saline or Tyrode solution produced no significant change in leucocyte counts. Preliminary experiments suggest that the leucocytes adhere to capillaries, especially in the lungs. The chemical nature of the active substances in solutions of lysed leucocytes has not yet been determined.
John F. Loutit

2746. **The Effects of Massage on the Circulation in Normal and Paralyzed Extremities**
K. G. WAKIM, G. M. MARTIN, J. C. TERRIER, E. C. ELKINS, and F. H. KRUSEN. *Archives of Physical Medicine* [*Arch. phys. Med.*] **30**, 135–144, March, 1949. 22 refs.

The object of this investigation was to determine the effect of massage on the blood-flow of the extremities in four groups of patients—those with normal muscles, those with lower motor neurone paralysis, those with upper motor neurone paralysis, and a small group with rheumatoid arthritis. The types of massage used were a modified Hoffa technique of deep stroking and kneading and a stimulating vigorous technique of very deep massage including friction. The blood flow before and after 15 minutes' massage was measured with a venous occlusion plethysmograph fitted with a compensating spirometer.

Vigorous stimulating massage produced a significant increase in blood-flow (over 15%) in 22 out of 26 observations on 15 normal subjects (average increase 45%). In 7 observations on 2 patients with flaccid paralysis a significant increase was obtained in all (average increase 103%). In 13 of these observations a further measurement was made 30 minutes after massage, and in all but 1 a significant increase was still present.

Deep stroking and kneading massage produced no significant increase in the blood-flow of the majority of normal subjects, or in those with spastic paralysis or rheumatoid arthritis. However, a significant increase was obtained in 4 out of 6 subjects with flaccid paralysis. In no case was any significant change noted in the blood-flow of the contralateral unmassaged extremity.
Andrew Zinovieff

2747. **An Evaluation of the Question of Anoxia in Fever Therapy**
E. E. GORDON, R. C. DARLING, and E. SHEA. *Archives of Physical Medicine* [*Arch. phys. Med.*] **30**, 154–163, March, 1949. 2 figs., bibliography.

The question of generalized anoxia during the application of physical hyperthermia at 104° to 106° F. (40° to 41·1° C.) was investigated in 18 subjects by assessing changes in pulse rate and in arterial-blood gas content. There was no evidence of anoxic anoxia, but the clinical observation of cyanosis and mental confusion suggests the possibility of ischaemic anoxia. Hyperventilation alkalosis was noted, and in this respect it is suggested that sedation may be of help. Routine oxygen therapy, however, is of limited theoretical value.
Andrew Zinovieff

Medical Jurisprudence

2748. **Serous Exudation in the Liver in Cases from Medico-Legal Practice.** (Серозный отек печени по материалам судебно-медицинской практики)
A. V. Rusakov. Архив Патологии [*Arkh. Patol.*] **11**, No. 1, 55–59, Jan.–Feb., 1949. 3 figs., 4 refs.

Oedema of the gall-bladder wall has been found frequently in cases of death from drowning. It has also been seen in cases of death from electric injury and dichlorethane poisoning. A constant finding in such cases was dilatation and oedema of the spaces of Disse in the liver. It is known that Disse's spaces communicate with perihepatic lymphatics and that the latter are continuous with the lymphatics in the gall-bladder wall. It is therefore suggested that oedema of the gall-bladder wall in cases due to drowning follows right-sided heart failure with raised venous pressure in the hepatic circulation. In cases of electric shock the mechanism may be arterial, capillary spasm driving fluid from the liver sinusoids into Disse's spaces. The appearance of oedema in cases of dichlorethane poisoning may be explained by increased permeability of the endothelium separating the sinusoids from Disse's spaces. *L. Crome*

2749. **Injuries and Death from Lightning**
M. J. G. Lynch and P. H. Shorthouse. *Lancet* [*Lancet*] **1**, 473–478, March 19, 1949. 5 figs., 24 refs.

The elements of the lightning flash which may produce injury are: (*a*) the direct effect of the current, (*b*) the superheated air, and (*c*) the expanded and repelled air. The last factor is responsible for the damage to clothing and may hurl the body several yards. It may also cause injuries fatal in themselves. Lightning burns are of three types: (*a*) linear burns, (*b*) arborescent burns, and (*c*) surface burns beneath metallic objects. Usually a person struck by lightning falls unconscious immediately. This may be due to syncope or concussion. While unconscious the victim usually lies immobile, and there is none of the restlessness, tremor, twitching, or convulsions which are common in unconsciousness due to electric shock. The unconsciousness may amount to suspended animation, the cardiac and respiratory centres being paralysed. Atropine and adrenaline by intracardiac injection, combined with artificial respiration and lumbar puncture, are recommended when the heart has stopped. When consciousness has been regained, the commonest abnormality is paraplegia. There is complete flaccid paralysis from the waist downwards with partial or complete sensory loss. Both sensation and motor power return within 12 to 24 hours. Many other secondary effects of a trophic nature and of autonomic origin may be observed. Retrograde amnesia is common, there may be psychological changes, and painful muscular cramps may occur. Remote neurological sequelae are rare. Hemiplegia, aphasia, choreoathetosis, spinal atrophic paralysis, and mixed types resembling disseminated sclerosis or general paralysis have been reported. Arteriosclerosis appears to be a predisposing factor in the development of disease of the central nervous system after lightning or electric shocks.

The authors describe an incident in which lightning struck a football ground, killing 2 players and affecting 2 more less seriously. In the fatal cases they found singeing of the hair, subcutaneous haemorrhages, and arborescent marks in the skin. The veins were engorged, there were haemorrhages on the lungs and pericardium, retroperitoneal haemorrhage, and haemorrhage into the pancreas. There were also minute haemorrhages in the floor of the fourth ventricle. Histologically, they found various degrees of necrosis of the pancreas, particularly in the tail, the cellular elements being quite unrecognizable in the more seriously affected parts. In the floor of the fourth ventricle haemorrhages were seen ranging from 2 to 3 mm. in diameter to microscopic perivascular extravasations. Small haemorrhages occurred in other parts of the brain. The authors contrast their histological findings with those described in previously reported cases. *Gilbert Forbes*

2750. **Results of Examination in 732 Cases of Rape.** (Untersuchungsergebnisse an 732 Vergewaltigungen)
P. Schrank and K. H. Koch. *Zeitschrift für Geburtshülfe und Gynäkologie* [*Z. Geburtsh. Gynäk.*] **130**, 200–213, 1949. 5 figs., 26 refs.

Of 732 cases of alleged rape studied at the Obstetrical-Gynaecological Clinic of Heidelberg University, 81·5% occurred in 1945, 18% in 1946, and 0·5% during the first 16 weeks of 1947. The age of the victims varied from 12 to 52 years. Four of them were menopausal and 11 were already pregnant at the time of the act. In 469 cases conception was alleged to be the result of the violation, 242 women having become pregnant for the first time. In 146 cases the pregnancy was terminated for "ethical reasons". In 73 cases, amenorrhoea ("fright-amenorrhoea") not due to pregnancy resulted.

Of the pregnant women 284 were able to supply exact details of their menstrual cycles and the date of cohabitation. Of these, 214 menstruated at fairly regular intervals of 26 to 30 days, and 103 of these conceived within the Knaus-Ogino "optimum period", 46 during the postmenstrual period, and 65 during the premenstrual period.

[Linzenmeier (*Zbl. Gynäk.*, 1947, **69**, 1108) studied a similar though smaller series at Karlsruhe and found that out of 48 women with regular 4-weekly periods 23 conceived during the postmenstruum, 25 during the intermenstruum, corresponding to the "optimum period", and not one during the premenstruum. In none of the women who did not conceive as a result of the enforced cohabitation had the act taken place during the optimum period.] *N. Alders*

Radiology

2751. **Studies with Colloids Containing Radioisotopes of Yttrium, Zirconium, Columbium, and Lanthanum. I. The Chemical Principles and Methods Involved in Preparation of Colloids of Yttrium, Zirconium, Columbium, and Lanthanum**
J. W. GOFMAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 297–304, March, 1949. 5 refs.

From the Department of Physics of the University of California the author describes the chemical principles involved in the preparation of colloids incorporating radio-isotopes of yttrium, zirconium, columbium, and lanthanum. These substances were chosen because of the availability of radio-isotopes of a wide range of nuclear properties (half-life, type of decay, radiation energy) and because of the ease with which the chemical structure and particle size of their colloids may be varied. [For details of the processes employed the original paper should be consulted.] *A. S. McLean*

2752. **Studies with Colloids Containing Radioisotopes of Yttrium, Zirconium, Columbium, and Lanthanum. II. The Controlled Selective Localization of Radioisotopes of Yttrium, Zirconium, and Columbium in the Bone Marrow, Liver, and Spleen**
E. L. DOBSON, J. W. GOFMAN, H. B. JONES, L. S. KELLY, and L. A. WALKER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 305–312, March, 1949. 3 figs., 4 refs.

The authors describe the selective localization in certain tissues of colloids such as those described in the preceding paper [see Abstract 2751].

Colloids having the common property of localizing in the liver and spleen of mice, rats, and rabbits are those of a " relatively large " particle size. In general, the disappearance rate of intravenously injected colloid from the blood stream is rapid, the half-time for blood clearance being ½–1 minute. It is thus certain that much of the colloid is cleared in a single passage through the liver, but the mechanism responsible for this rapid uptake is not clear. All of these colloids contain a small percentage of components which clear more slowly from the blood stream. From the methods of preparation polydispersity of the sols is to be expected, and the smaller particles are responsible for this slowly clearing fraction. Colloids localizing primarily in the bone marrow are of the zirconium-hydroxy-lactate and yttrium-hydroxy-citrate type and have a much smaller particle size. They disappear slowly from the blood stream, the half-time for clearance being 30 to 80 minutes. After bone marrow, the liver and spleen receive the next highest quantity, the liver specific activity being approximately one-third that of the marrow. The bulk of the yttrium and zirconium colloids of both types tends to remain localized at the site of deposition for periods of at least 2 to 4 weeks.

The distribution of these colloids and the availability of radio-isotopes of a wide range of nuclear properties render them suitable for experimental studies requiring specific irradiation of the liver, spleen, and bone marrow, and also for therapeutic use in certain neoplastic diseases of the haemopoetic system and liver. *A. S. McLean*

2753. **An Experimental Study of the Effect of Zirconium and Sodium Citrate Treatment on the Metabolism of Plutonium and Radioyttrium**
J. SCHUBERT. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 313–325, March, 1949. 6 figs., 9 refs.

A study was made of the effect of a single dose of zirconium citrate on the excretion and distribution of plutonium and radio-yttrium in rats and a growing dog. It was found that early administration of zirconium citrate to rats increased the excretion of plutonium from 1% to 50% and that of radio-yttrium from 25% to 60% of the injected dose during a 24-hour period. The amount of plutonium and radio-yttrium deposited in the skeleton was reduced by factors of 6 and 2·6 respectively. No significant changes in the plutonium or radio-yttrium contents of the faeces, liver, spleen, or kidney were found. Administration of zirconium citrate to a dog 5 months and 2½ years after exposure to plutonium was followed by a sustained increase in the excretion rate. The extent of the increase was proportional to the dose of zirconium citrate.

A discussion is given of the chemical concepts involved in applying metal displacement principles to the removal of radioactive metals from the body.—[Author's Summary.]

2754. **Humoral Transmission of a Roentgenbiological Effect in Parabiosis.** (О гуморальной передаче рентгено-биологического эффекта в паравиозе)
I. V. KOLPAKOV and V. I. KHODOS. Архив Патологии [*Arkh. Patol.*] **11**, No. 1, 25–31, Jan.–Feb., 1949. 3 figs., 13 refs.

When two animals are joined together in parabiosis, and one of them irradiated while the second is protected from the effects of the *x* rays, the same blood changes, namely, initial leucocytosis followed by leucopenia, develop in both of them. If a single animal is irradiated and then joined to another in parabiosis, the irradiated animal will develop the usual pathological blood changes but its partner retains a normal blood picture. When irradiation is carried out very early after parabiosis, the protected animal shows no blood changes, proving that a well vascularized connexion is needed for the transmission of the leucopenic factor. If parabiotic connexion between two animals is severed 20 minutes after the irradiation of one of them, typical blood changes develop in both animals. *L. Crome*

2755. **The Study of Connective-tissue Reaction to Radiation. The Sieve or Chess Method**
B. JOLLES. *British Journal of Cancer* [*Brit. J. Cancer*] **3**, 27–31, March, 1949. 6 figs., 9 refs.

The author describes a new technique for the study of the reaction of tumour connective tissue to radiation. Advanced, inoperable breast tumours and tumours of the skin which were not amenable to radical surgery or radiotherapy were used in the investigation. If possible, a special mould applicator was built for each case, the lesion being reproduced by means of a stent impression in a plaster cast. Into this applicator, a lead sieve or "chess" was fitted tightly over the part to be treated, the sieve having circular or square apertures of diameters varying from 1 to 2 cm. and the thickness of the lead allowing 3% of the radiation to pass through. Radiation was delivered at right angles and every precaution taken to avoid shifting of the sieve. Material for histological examination was taken from both protected and exposed sectors (marked with gentian violet paint) before starting treatment and at varying intervals thereafter. Preliminary results in 9 cases show that connective-tissue reaction occurs not only in the irradiated areas, but also in the adjacent protected areas.

A. S. McLean

RADIOTHERAPY

2756. **Lessons to be Learnt from the Failures of Contact Therapy of Skin Epitheliomata.** (Quelles leçons tirer des échecs de la radiothérapie de contact des épithéliomas cutanés ?)
P. CHATTON. *Journal de Radiologie et d'Electrologie* [*J. Radiol. Electrol.*] **40**, 251–260, 1949.

The author describes 137 cases of cancer of the skin of the face, together with a few others, treated at the Montpellier Centre by contact therapy. The cases were divided into small groups because of variations in pathology and because some patients had received treatment elsewhere. Among 59 uncomplicated cases treated with a single field, 4 either failed to respond or had a recurrence, and of 17 cases which needed multiple fields 5 were not cured. In the complicated cases there were 3 failures out of 19 treated by single field, and 7 out of 17 treated by multiple fields. Radionecrosis was rare, but was observed in a few cases.

It is concluded that it is of the utmost importance that the size of the tumour be correctly estimated, and that a field large enough to extend at least 0·5 cm. beyond the estimated size must be used. The dose must also be received to a depth of 0·5 cm. under the tumour, and the falling dose at the periphery must be remembered. High doses are needed; therefore the radiation must be fractionated and filtered. *M. C. Tod*

2757. **Radium in Postnasal Lymphoid Hyperplasia and Infections**
H. B. DAMRON. *Journal of the Tennessee State Medical Association* [*J. Tenn. med. Ass.*] **42**, 317–321, Sept., 1949. 3 figs., 9 refs.

2758. **Intra-abdominal Contact Therapy.** (Über intra-abdominäle Nahbestrahlungen)
H. DRESCHER. *Strahlentherapie* [*Strahlentherapie*] **78**, 503–510, 1949. 17 refs.

In this report from Mayer's clinic at Tübingen, after a preliminary review of the principles and apparatus involved in contact therapy, the author describes the technique of intra-abdominal irradiation after palliative surgery for inoperable cancer of the female genital tract. Physical factors of the irradiation technique are 50 kV, 2mA, and 20 to 40 mm. focus-skin distance with no added filtration. The size and number of the fields and the focus-skin distance varied with the area and depth of the residual masses treated. The surface dose was 11,400 r in the majority of cases, but varied from 7,600 r to 15,200 r. The time of irradiation was usually from 1 to 4 minutes. Post-operative external irradiation is advised because of the possible presence of microscopic tumour particles.

Of the 27 patients, 3 survived for 3 or more years. Of the remainder 5 died post-operatively (3 of peritonitis, 1 of pulmonary embolus, and 1 of heart failure). A further 3 patients died several weeks after the operation (1 of peritoneal carcinomatosis, 1 of diffuse pelvic infiltration, and 1 of pulmonary oedema). A further 11 patients died within a year and 4 within the second year, 1 being untraced. Commenting on the high proportion of post-operative and late post-operative deaths, the author considers the incidence of peritonitis to be that usually attending such an operation and not to be due to necrosis of the treated part. In addition the author stresses the absence of danger to the surrounding organs, because of the low penetrating power of the rays.

Basil A. Stoll

2759. **Clinical Features and Treatment of Carcinoma of the Auricle.** (Beitrag zur Klinik und Therapie der Ohrmuskelcarcinome)
W. HORNBERGER. *Strahlentherapie* [*Strahlentherapie*] **79**, 207–232, 1949. 12 figs., bibliography.

A series of 59 cases of carcinoma of the auricle seen during the last 10 years is reviewed; 30 tumours were squamous-cell and 16 basal-cell, in contrast to the usual predominance of the latter in most series. This difference is attributed to the patients' rural origin. Males were twice as commonly affected as females. In the group of patients with basal-cell tumours treated by irradiation there was only 1 failure, in a case with 11 recurrences; recurrences in at least 3 other cases were successfully treated by further irradiation, and the prognosis in this type is therefore good. In the squamous-cell group the results of irradiation were comparatively poor, with 14 failures; lymph-node metastasis occurred in 6. Involvement of the meatus worsens the prognosis. In the "metatypical" and mixed-cell group, treatment by irradiation led to 1 failure in 5 cases. There were 3 failures among 4 patients previously irradiated for lupus ("lupus carcinoma"). In the melanoma group, treated by combined surgery and radiation, there was 1 failure in 4 cases.

Both *x* rays and radium were used, but technical details are not given. Short-distance *x*-ray therapy (method of Chaoul) has great advantages over deep *x*-ray and radium therapy and is now almost always used. The importance of the cartilage is discussed; it is highly resistant to invasion by carcinoma, unless the perichondrium is damaged and destroyed by infection when invasion and necrosis take place. For early cases treatment by irradiation alone is advised; for recurrence of basal-cell lesions, further irradiation should be used, with surgery for later recurrences. For recurrence of squamous lesions, surgery is usually needed; lesions threatening the meatus or spreading on to the scalp, or arising on lupus, should be treated by surgery. Sulphonamide powder is a useful prophylactic against infection. For perichondritis and cartilage necrosis the part involved should be excised unless healing is spontaneous. For secondary nodes irradiation should be combined with surgery. In cases of melanoma biopsy is better avoided and radical irradiation used, with surgery as a good alternative. *J. Walter*

2760. **The Role of Nitrogen Mustard (HN2) as a Systemic Adjunct to the Radiation Therapy of Certain Malignant Diseases**
B. Roswit and G. Kaplan. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **61**, 626–636, May, 1949. 7 figs., 18 refs.

A group of 87 patients receiving irradiation for malignant disease was studied; most of them had Hodgkin's disease, lymphosarcoma, chronic leukaemia, or bronchogenic carcinoma. Methyl bis- (β-chloroethyl)amine hydrochloride was used during those periods when radiotherapy was contraindicated, the drug not being given, however, in the presence of severe bone-marrow depression. A dose of 0·1 mg. per kg. body weight was injected daily in an infusion of normal saline for four consecutive days; the course was not repeated until the leucopenia caused by the drug had disappeared. Thrombophlebitis occurred after repeated injections but could sometimes be avoided if injections were not made into limbs whose circulation was obstructed by tumour or large lymph nodes. Nausea and vomiting occurred 1 to 8 hours after the first injection but became less subsequently. Substances which allay radiation sickness had no effect, but preliminary sedation and overnight fasting helped to prevent gastro-intestinal symptoms.

Leucopenia occurred in 65% of cases, but this and bone-marrow depression disappeared in 4 weeks. The degree of leucopenia increased with each course. Penicillin was used if agranulocytosis occurred. Toxic psychosis was observed in one case. Only 10% of men had active spermatogenesis after treatment. In a control group treated by other methods 43% had no testicular atrophy. In some cases the damage due to nitrogen mustard was permanent.

In Hodgkin's disease 85% of patients benefited by one course. The remission was for from 1 to 16 weeks, averaging 7 weeks. The greater the number of courses given, the less the response. Of 6 cases of lymphosarcoma 2 responded well, and 2 out of 4 patients with reticulosarcoma improved. Good results were not obtained in leukaemia. One out of 2 patients with mycosis fungoides had very temporary relief. Other malignant conditions showed little change. In 9 out of 16 cases of bronchogenic carcinoma there was symptomatic and radiological improvement for a few weeks.

It is concluded that nitrogen mustard is useful for palliation in advanced Hodgkin's disease and other lymphomata, but should not be used in early cases of localized disease. It should not be used as maintenance therapy in malignant lymphomata, including chronic leukaemia, for cumulative systemic intoxication leads to aplasia of the bone marrow and testicular atrophy. *M. I. R. Knox*

See also Sections Dermatology, Abstract 2934; Neurology, Abstract 2991.

RADIODIAGNOSIS

2761. **Radiological Study of Cerebral Cisternae in Normal Conditions.** (Studio radiologico delle cisterne cerebrali in condizioni normali)
G. Lombardi. *Radiologia Medica* [*Radiolog. med., Torino*] **35**, 395–409, May, 1949. 16 figs., 10 refs.

The author describes a special technique for the demonstration of the various cerebral subarachnoid cisternae. This is a modification of Graeme Robertson's method of encephalography.

[The article is well illustrated and the details are easy to follow. It should be of special interest to neurosurgeons and neuroradiologists.] *A. Orley*

2762. **Minimal Tuberculosis. Problems in Roentgenologic Interpretation**
I. D. Bobrowitz and A. Hurst. *Radiology* [*Radiology*] **52**, 519–532, April, 1949. 22 figs., 8 refs.

The authors studied 220 patients in a sanatorium to determine the clinical significance and prognosis of minimal pulmonary tuberculous lesions of the "reinfection type". They first of all stress the importance of complete visualization of the lesion, and suggest that in many cases special views such as lordotic or apical projections are necessary. They attempted to divide lesions into four groups—exudative, productive-fibrotic, exudative-productive, and fibro-calcific. Such classification was extremely difficult, not only because differences in technique altered the radiological shadow, but because there was also considerable variation in classification between individual observers. They point out the importance of referring to radiographs taken earlier in the course of the disease, as it is impossible in cases of reinfection to decide the prognosis and clinical significance of a lesion on the basis of one film only. In some cases with minimal lesions at the time of the present investigation, study of previous films revealed that the disease had been more extensive or that cavitation had been present. Frequently linear scars and rounded foci, or more rarely stellate scars, had resulted from cavity closure, and thus the risk of reopening a cavity was

always present. In some cases lesions classified as of the productive and fibrotic type progressed rapidly; in others with hard rounded foci central softening was present. Correlation of the *x*-ray appearances with the clinical condition, symptomatology, and bacteriological findings was frequently helpful in assessing the degree of activity.

In their previous study of minimal tuberculosis these authors found that in most cases the disease progressed during the first 2 years of the follow-up period, the progression rate being highest in the second year and constituting a risk of some importance in the third year; therefore the need for closely and constantly following up all patients with minimal lesions is very evident.

L. G. Blair

2763. **Radiological Examination of the Pulmonary Apices.** (L'examen radiologique des sommets pulmonaires)
G. J. MELOT. *Acta Clinica Belgica* [*Acta clin. belg.*] **4**, 93–103, March–April, 1949. 6 figs., 17 refs.

It is pointed out that the standard postero-anterior projection used for chest radiography has certain limitations so far as apical structures are concerned. The clavicles may superimpose shadows and make interpretation difficult. Calcification in the upper costal cartilages, soft-tissue swellings such as substernal goitres, and low-lying cervical nodes may also obscure the picture. Two supplementary views are therefore recommended which are taken with the patient supine. The first projection—cranio-caudal—throws the clavicle shadows downwards: about 25 degrees tilt of the tube is necessary. The second projection—caudo-cranial—is also taken with the patient supine. It may be necessary to take two or three pictures with different tube tilts: 30, 40, and 50 degrees are recommended. By this means the shadow of the clavicle is thrown upwards above the extreme apex of the lung.

The author describes 2 cases to illustrate the value of these projections, particularly the caudo-cranial one. In the first case the tilted projection confirmed the presence of a tuberculous cavity which was doubtful in the standard postero-anterior view; in the other the attachment of an apical adhesion in a pneumothorax is made clear.

Tomography is also effective, but these two tilted views are cheaper and quicker and often make tomography unnecessary. *J. W. D. Bull*

2764. **Mass Roentgenological Survey of the Gastro-intestinal Tract to Detect Cancer of the Stomach**
S. MOORE. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **61**, 470–474, April, 1949. 3 figs., 4 refs.

The author first analyses the incidence of gastro-intestinal cancer according to the gastro-intestinal segment involved and also according to age, and concludes that the art of gastro-intestinal examination, in its present state, must still remain an art and therefore unsuitable for mass survey techniques. Although cancer might possibly be detected by this method, only the late cases would probably be discovered. Only a small proportion of gastro-intestinal tumours can be detected by mass survey methods. From the data which have been accumulated it is obvious that the incidence of carcinoma of the stomach has been exaggerated. It is, of course, true that different data will be found in different clinics, but on the whole the incidence of cancer is very much higher for the female breast, the uterus, and the lungs. *A. Orley*

2765. **Gastro-intestinal Food Hypersensitivity: Roentgenographic Demonstration**
E. J. TALLANT, H. A. O'NEILL, F. URBACH, and A. H. PRICE. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **16**, 140–150, April, 1949. 4 figs., bibliography.

A review of the pertinent literature suggests that the small intestines are intimately involved in the production of symptoms of gastro-intestinal food hypersensitivity. The authors describe a radiographic method which allows the evaluation of the changes in the small intestines in sensitive and non-sensitive patients. In a group of 12 patients who presented symptoms of food hypersensitivity, feeding with a mixture of barium and the specific allergen produced narrowing and segmentation of the small intestines and scattering of the meal. These changes did not occur after the administration of a barium–water mixture. No abnormalities in the small intestines could be detected in hypersensitive patients in whom the allergic disturbance did not involve the gastro-intestinal tract. The abnormal changes in the small intestines are in themselves non-specific, and acquire diagnostic significance only when a control examination with a simple barium–water mixture after a sufficient lapse of time yields a normal radiographic picture.

A. Orley

2766. **Double Contour, Cupping and Spurring in Roentgenograms of Long Bones in Infants**
K. GLASER. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **61**, 482–492, April, 1949. 10 figs., 5 refs.

Radiographic examination of the long bones was carried out at monthly intervals from birth to 8 months of age in 100 healthy prematurely born infants. A double line in the contour of the long bones of the extremities and a cupped and spurred appearance of the epiphysial lines of the same bones were frequently observed. Similar changes are sometimes also seen in full-term infants. No pathological changes were found on histological examination of the involved bones obtained either by biopsy or at post-mortem examination The changes, which are most frequently observed between the ages of 2 and 6 months, disappear spontaneously later in life, and their appearance in a radiograph of the long bones taken during the process of growth must therefore be considered as normal. *A. Orley*

See also Section Medicine: General, Abstract 2821.

Pathology

EXPERIMENTAL PATHOLOGY

2767. **Studies on the Hemolysis of Human Erythrocytes by Homologous Complement in the Presence of Tannic Acid**
J. L. PECK and L. THOMAS. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **84**, 216–237, March, 1949. 12 refs.

Human erythrocytes treated with tannic acid are haemolysed in the presence of human or guinea-pig complement under the following conditions: (*a*) The diluent used is 0·7% sodium chloride. (Higher concentrates inhibit the preparation of erythrocytes with tannic acid and may prevent haemolysis of treated cells in the presence of complement.) (*b*) Isotonic glucose is used as diluting fluid instead of 0·7% NaCl. (*c*) A concentration of tannic acid between 0·12 and 0·015% is used. (With these concentrations the time required to sensitize the erythrocytes varies inversely with the concentration of tannic acid.) (*d*) A 1% suspension of erythrocytes is used at *p*H 7 to 8. (*e*) Components are added in the order: erythrocytes, tannic acid, wait 5 minutes to sensitize, add complement.

Evidence is provided that in this reaction the effective material in human and guinea-pig serum is probably complement; that tannic acid is absorbed by erythrocytes and by serum; that pre-treatment of erythrocytes with serum will prevent their being so altered by tannic acid that they are sensitized to complement; that little complement is absorbed by tannic-acid-sensitized erythrocytes, but that such cells, though more susceptible to haemolysis by further added complement, will not haemolyse if the complement is removed by washing; and that washing does not alter the complement-sensitivity of tannic-acid-treated cells. *C. L. Oakley*

2768. **Quantitative Interference with Estrogen-induced Tissue Growth by Folic Acid Antagonists**
R. HERTZ and W. W. TULLNER. *Endocrinology* [*Endocrinology*] **44**, 278–282, March, 1949. 2 figs., 8 refs.

It has previously been shown (Hertz, *Endocrinology*, 1945, **37**, 1) that the genital tract of the chick or monkey fed on diets deficient in folic acid makes a very limited response to the administration of high doses of oestrogen. A similar reduction of growth-rate occurs when a crude folic acid antagonist is added to the food. The present paper describes a quantitative study of the inhibition by chemically pure folic acid antagonists of oestrogen-induced growth in the genital tract of chicks and rats.

Newly hatched chicks were given no food, but unlimited water, for 6 days. On the first 3 days different groups of chicks were injected with varying doses of a folic acid antagonist, and on the 4th and 5th days each chick received an injection of 1 mg. of diethylstilboestrol dissolved in 0·2 ml. corn oil. After a further day the genital tracts were removed and weighed. Groups of chicks receiving oestrogen alone, folic acid antagonist plus folic acid, and no treatment at all were used as controls. In the second experiment female rats, 3 weeks old, were subjected to ovariectomy and fed on a standard ration with the addition of 2% of dried liver. After 3 to 5 days each rat received, by subcutaneous injection, a dose of folic acid antagonist on 3 consecutive days. On the 2nd and 3rd of these days 10 μg. of oestradiol dissolved in 0·5 ml. of water was injected into each rat and after a further day the animals were killed and their uteri weighed.

Tests were made of 8 folic acid antagonists, all compounds closely related in structure to folic acid itself, but most of the work was carried out with 4-aminopteroylglutamic acid. The experimental findings with this substance are presented graphically; increasing doses of 4-aminopteroylglutamic acid (from 4 to 16 μg.) caused progressive diminution in weight of the genital tracts of both chicks and rats after ovariectomy. The results obtained with the 7 other folic acid antagonists are collected in a table. Growth inhibition in the female genital tract was caused by 4-amino-N^{10}-methylpteroylglutamic acid and 4-amino-pteroylaspartic acid, while 4-desoxy-pteroylglutamic acid was moderately effective. On the other hand, four derivatives of pteridine, uncombined with an amino-acid, proved ineffective. It is suggested that this interference of hormone action by anti-vitamins may be of significance in therapy by reducing the effectiveness of endogenous hormones, for example, in prostatic carcinoma. *H. G. Crabtree*

2769. **Cytoplasmic Inclusions and the Characteristics of Hodgkin's Diseased Lymph Nodes in Tissue Culture**
C. G. GRAND and R. CHAMBERS. *Cancer Research* [*Cancer Res.*] **9**, 183–192, March, 1949. 14 figs., 19 refs.

The authors cultivated various pathological and normal human lymph nodes on Maximov double coverslips and in Carrel flasks in mixtures of human serum, fowl plasma, and chick embryo extract. Altogether, 87 lymph nodes involved in Hodgkin's disease at various stages and 25 affected by lymphosarcoma, 21 by leukaemia, 26 by metastatic carcinoma, 15 by non-specific lymphadenitis, as well as 23 normal lymph nodes, were cultivated for periods of a few days to several weeks without sub-culturing.

Cultures were stained vitally with 1 in 50,000 brilliant cresyl blue in Ringer's solution or fixed at intervals and stained with Giemsa solution, Sellers's virus stain, or haematoxylin. Outgrowth from lymph nodes in Hodgkin's disease at an early stage was mainly lymphocytic; that from nodes in which the disease was more advanced consisted mainly of reticular cells (macrophages) and multinucleate giant cells. The latter contained 3 to 5

nuclei and appeared early, close to the explant; they were regarded as Sternberg-Reed cells. From nodes in the late fibrotic stage only fibroblasts grew. Cellular degeneration and liquefaction of the medium was marked, especially when reticular cells were numerous. In cultures of normal lymph nodes, and pathological lymph nodes other than those from cases of Hodgkin's disease, outgrowth was mainly lymphocytic; reticular and giant cells were rare and cellular degeneration and liquefaction of the medium were slight or absent.

After 15 minutes' vital staining of cultures of lymph nodes from cases of Hodgkin's disease with brilliant cresyl blue, cytoplasmic inclusions were visible in reticular and giant cells, in lymphocytes, and occasionally in fibroblasts. These were also demonstrable in fixed preparations by Sellers's stain. They appeared to consist of groups of small bodies within vacuoles. They were not seen in cultures of normal nodes or of any of the other pathological lymph nodes examined. When cultures of normal nodes were treated with supernatant fluids from flask cultures of nodes involved in Hodgkin's disease, similar inclusion bodies appeared in them and the general character of growth approximated to that of cultures from cases of Hodgkin's disease, except that no giant cells appeared. *M. H. Salaman*

2770. **Factors Influencing Collagen Content in Experimental Cirrhosis**

T. G. MORRIONE. *American Journal of Pathology* [*Amer. J. Path.*] **25**, 273–285, March, 1949. 7 figs., 8 refs.

Hepatic cirrhosis was induced in rats by intermittent exposure to carbon tetrachloride vapour over a period of 35 days. The hepatic collagen was estimated at intervals, and the rate of production was found to give a curve of exponential type. After 35 days the carbon tetrachloride was discontinued and the animals were put on a series of different diets. Decrease in collagen content was found in those on normal diets and also in those receiving a low-protein diet with added methionine, choline, or cystine. No such diminution was found in those receiving high-fat–low-protein diets, nor was it observed in those whose portal vein had been ligated. From this investigation it appears that resorption of collagen is dependent on the functional integrity of the parenchymal cells. *R. H. Heptinstall*

2771. **Acute Experimental Calcium Chloride Acidosis**

A. D. T. GOVAN and J. PARKES. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **30**, 105–114, April, 1949. 10 figs., 24 refs.

Administration of ammonium chloride to rabbits in doses of 0·75 g. per kg. leads to acidosis and death in about 4 days: necrosis of the renal tubules is widespread. The possibility that the death of such animals might be due to uraemia was rendered doubtful by the relatively low blood urea level (173 mg. per 100 ml. or less) and the high urinary fluid and nitrogen output. In order to examine the effect of severe acidosis without the complicating effect of the ammonium ion the authors administered a 10% solution of calcium chloride by stomach tube to healthy rabbits, giving total amounts varying from 1·5 to 2·5 g. per kg.

The animals so treated fell into two distinct groups—those given 1·5 to 2·2 g. per kg., and those given 2·5 g. per kg., with a small overlap. In the first group the most striking change was a reduction in the carbon-dioxide-combining power of the blood from 40 to 13·5 vols. %; the level of blood urea was only slightly increased, that of blood cholesterol doubled; blood *p*H fell slightly; no ammonia could be detected in the blood. Histological examination of killed animals showed emphysema of the lungs with small areas of collapse associated with numerous fat emboli; eosinophil leucocytes had accumulated in the alveolar capillaries and formed nodules round the emboli; the kidney glomeruli appeared larger than usual and there were adhesions between the tuft and Bowman's capsule; catarrhal changes were present in the first convoluted tubules.

Animals receiving 2·5 g. per kg., unlike those receiving less, showed well-marked symptoms, becoming drowsy, palsied, and incoordinated until they died in coma. The blood changes observed in the other group were all present to a more pronounced degree, with a marked increase in the blood urea and blood ammonia levels and in the plasma lipid content. Beside the histological changes observed in the first group, fine fatty degeneration was apparent in the myocardium, the liver glycogen content was greatly diminished, and focal degenerative changes were present in the midzone of most lobules. The renal changes were more severe, the first convoluted tubules and descending limbs of Henle's loops showing catarrhal and even necrotic changes; the ascending limbs were dilated, the collecting tubules contained many colloid casts, and early necrosis was evident in many of them.

The authors conclude that the differences between calcium chloride and ammonium chloride poisoning are due to the higher toxicity of the ammonium ion, and that the severer changes in the second group of animals given calcium chloride are due to poisoning with ammonia, which the damaged liver has been unable to convert into urea. The authors also note that fat is mobilized from the depots before organ glycogen is exhausted, and that retention of phosphorus as compared with calcium occurs after administration of calcium chloride.

C. L. Oakley

2772. **Studies on Acute Disseminated Encephalomyelitis produced Experimentally in Rhesus Monkeys. IV. Disseminated Encephalomyelitis produced in Monkeys with their own Brain Tissue**

E. A. KABAT, A. WOLF, and A. E. BEZER. *Journal of Experimental Medicine* [*J. exp. Med.*] **89**, 395–398. April, 1949. 4 figs., 13 refs.

Six rhesus monkeys were subjected to unilateral frontal leucotomy; the excised brain substance was frozen in solid carbon dioxide until the animals had recovered from the surgical procedure, and then each received at weekly intervals three 1-ml. intramuscular injections of

their own brain compounded with aquaphor, paraffin oil, and killed tubercle bacilli. [Details of the preparation of this inoculum will be found in *Science*, 1946, **104**, 362; *J. exp. Med.*, 1947, **85**, 117.] In 5 of the animals one or more of the following symptoms developed: ptosis, dilatation of the pupils, reduced vision or blindness, intention tremor, ataxia, and fine generalized tremors; these monkeys were killed when moribund. The histological lesions found were typical of the acute disseminated process previously described after the use of species-specific but not autogenous material—namely, focal inflammatory lesions and areas of perivascular demyelinization throughout the central nervous system. The sixth monkey died of an acute inflammatory complication of the surgical procedure. *W. S. Killpack*

2773. **The Distribution of Radioactivity in Tumor-bearing Mice after Injection of Radioactive Iodinated Trypan Blue**
C. D. Stevens, A. Lee, P. H. Stewart, P. M. Quinlin, and P. R. Gilson. *Cancer Research* [*Cancer Res.*] **9**, 139–143, March, 1949. 1 fig., 19 refs.

The distribution of radioactivity in the tissues of 24 Swiss A mice, each bearing two subcutaneous implants of tumor 15091a, and 5 control mice, was measured after intravenous injection of a radioactive dye mixture prepared by iodination of trypan blue in the presence of radioactive iodide. The concentration of radioactivity was several times as high in tumour tissue as in skeletal muscle or skin, but less than that in the liver, spleen, or kidneys. The data are compared with those obtained by the use of radio-brominated trypan blue and Evans blue; the behaviour of these different radioactive dye preparations is similar. In tumour-bearing mice the liver consistently showed much more radioactivity than that of control mice. *I. Hieger*

2774. **The Use of Tracer Doses of Radioactive Iodine, I^{131}, in the Study of Normal and Disordered Thyroid Function in Man**
S. C. Werner, E. H. Quimby, and C. Schmidt. *Journal of Clinical Endocrinology* [*J. clin. Endocrinol.*] **9**, 342–354, April, 1949. 16 refs.

This report from Columbia University, New York, analyses the thyroid uptake of radioactive iodine in 267 patients suffering from various conditions, to whom 40 to 100 μc. I^{131}, standardized according to Marinelli, was administered orally in the non-fasting state. The percentage uptake of the dose by the thyroid was measured 24 hours later by means of a wide-aperture Geiger counter placed 15 cm. from the neck.

In 57 patients with normal thyroid function the uptake ranged from 7 to 49%; in only 6 cases, however, was the uptake more than 35%. The lowest values were found in women of the older age group. Of 97 patients with hyperthyroidism, 91 had an uptake exceeding 35%. The lowest values (13 and 15%) were found in cases in which hyperthyroidism had recurred after I^{131} therapy. The normal range is believed to be 10 to 35%, but there is some overlap between results in patients with normal thyroid function and those with hyperthyroidism. Of 21 patients with clinical remission of hyperthyroidism as a result of surgery or of treatment with propyl-thiouracil, *x* rays, or I^{131}, 8 had an uptake of more than 35%. Similarly, in 4 of 11 cases of non-toxic goitre, 4 of 8 cases of malignant exophthalmos, 3 of 7 cases of chronic thyroiditis, and 3 of 10 cases of pituitary eosinophil adenoma the uptake exceeded 35%. Cases of chromophobe adenoma of the pituitary, Addison's disease, Cushing's syndrome, obesity, anorexia nervosa, and carcinoma of the thyroid gave values in the normal or low-normal range. In hypothyroidism and acute thyroiditis the uptake was below 10%. *G. Ansell*

2775. **Diet and Resistance to Experimental Tuberculosis in Mice**
S. R. Sengupta and J. W. Howie. *British Journal of Nutrition* [*Brit. J. Nutrit.*] **2**, 313–320, 1949. 2 figs., 30 refs.

2776. **Production of Leukaemia by Intra-embryonic Inoculation of a Chloromyeloma in the Rat.** (Production de leucémies par inoculations intra-embryonnaires d'un chloro-myélome du rat)
C. Oberling, M. Guérin, and —. Lacour. *Comptes Rendus des Séances de la Société de Biologie* [*C.R. Soc. Biol. Paris*] **143**, 352–353, March, 1949. 1 ref.

MORBID ANATOMY

2777. **Arterio-venous Anastomoses of the Pulmonary Circulation. III. Critical Review of the Literature, in which Occluding Arteries have been Mistaken for Diseased Arteries.** (Об артерио-венозных анастомозах малого круга кровообращения. III. Критический обзор литературы, в которой нормальные "замыкающие артерии" принимаются за патологически измененные артерии обычного строения)
A. V. Ryvkind. Архив Патологии [*Arkh. Patol.*] **11**, No. 2, 9–16, March–April, 1949. 4 figs., 11 refs.

The previous two papers contained a full description of the arterio-venous communications in the lungs. The so-called "occluding arterioles" are the central parts of such communications. They are functionally active links between the bronchial artery, the pulmonary artery, and the bronchiolar plexus of veins. The intima of such occluding arterioles is formed by a thick longitudinal layer of muscle traversed by a network of fine elastic fibres. It is often many times thicker than the media of the vessel. The lumen may be patent or closed, depending on the functional state of the vessel. In view of these anatomical features, it is hardly surprising that many observers have in the past regarded such arterioles as arteriosclerotic or otherwise diseased. In the present communication the author reviews critically a number of papers in which the findings were misinterpreted in that way. The study of photomicrographs and detailed descriptions leaves little doubt that in many cases the authors were in fact dealing with occluding arterioles and not pathological states in arteries.
L. Crome

2778. **Pathological Features of Intrathoracic Tuberculosis in Clinically Healthy Adolescents.** (Патоморфологическая характеристика внутригрудных туберкулезных изменений у клинически здоровых подростков) M. G. IVANOVA. Архив Патологии [*Arkh. Patol.*] **11**, No. 2, 31–37, March–April, 1949. 2 figs., 19 refs.

The lungs of 100 adolescents, aged 14 to 19 years, dying from accidental causes were examined radiologically and histologically. In 26 cases there was no tuberculosis. Out of the remaining 74 with evidence of tuberculosis, 20 had a relatively fresh primary complex with or without wider spread, and 54 had old primary complexes in various stages of calcification. A more thorough histological examination of the material proved that apparent full calcification of foci in lung or lymph nodes is anything but a reliable indicator of complete healing. The presence of specific tuberculous granulation tissue was taken as a sign of activity, and this granulation tissue was found in 29 out of the 54 cases mentioned above when the material was examined by serial section.

The presence of primary complexes in 20 adolescents pointed to the relative frequency with which primary infection occurs in this age group. Furthermore, when compared with primary infection in childhood, it was accompanied more frequently by lymphatic and haematogenous spread. This spread of infection was seen in the apices and the mediastinal lymph nodes, and there was also occasional reactivation of the primary foci with peripheral extension of the lesion. *L. Crome*

2779. **Dilatation of the Veins of the Sciatic Nerve.** (Расширение вен седалищного нерва) E. M. MARGORIN. Архив Патологии [*Arkh. Patol.*] **11**, No. 2, 37–43, March–April, 1949. 3 figs., 17 refs.

Sciatic nerves were examined in a series of 40 necropsies. Dilatation of endoneural and epineural veins was seen in 12 preparations. This dilatation did not always coexist with subcutaneous varicose veins. In two of the advanced cases, in which the venous ectasia amounted to gross varicosity, degenerative changes were also seen in the nerve fibres. *L. Crome*

2780. **Endophlebitis Hepatica Obliterans.** [In English] G. TEILUM. *Acta Pathologica et Microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **26**, 157–166, 1949. 8 figs., 21 refs.

A woman of 36 years suffered from increasing abdominal distension, nausea, and oliguria for 3 weeks. She had also had a febrile attack and diarrhoea lasting for 3 days some 3 months previously. There was slight yellow discoloration of the sclerae but not of the skin. There was marked ascites and after paracentesis the firm edge of the liver was felt 2 finger-breadths below the costal margin. Five days after paracentesis the ascites had returned and cyanosis and oedema of the left arm were now noted. Death occurred 4 days later.

Necropsy revealed recent thrombosis in the axillary vein, the subclavian vein, and the lower part of the internal jugular vein of the left side. There was congestion of the veins of the stomach and of the lower part of the oesophagus. There was also thrombosis of the inferior vena cava proceeding from the hepatic veins. The liver measured $21 \times 18 \times 10$ cm. [the weight is not given] and was of dark, bluish-red colour. The capsule was thickened. The cut surface showed a distinct nutmeg pattern and the consistency was markedly firm. The large branches of the hepatic vein were almost completely occluded by thrombus, and a firm whitish-yellow infarct was present. The portal vein also contained thrombus. Histological examination showed marked venous congestion of the liver and endophlebitis of the hepatic veins. In the smaller branches of the veins there was proliferation of the endothelium, and in the larger branches fibrosis. *R. B. Lucas*

2781. **Distribution of the Lymphatics of the Human Kidney as Shown in a Case of Carcinomatous Permeation** A. J. RAWSON. *Archives of Pathology* [*Arch. Path.*] **47**, 283–292, March, 1949. 5 figs., 5 refs.

The distribution and arrangement of the lymphatic channels was studied in a kidney obtained at necropsy in a case of extensive carcinoma. Widespread lymphatic permeation was found throughout the body. No tumour nodules had formed, the neoplastic cells being confined to the lymphatic vessels. Microscopical examination of the kidney showed that the lymphatic vessels were clearly visible and distended by solid cords of tumour cells. In serial sections stained by haematoxylin and eosin the neoplastic cells were conspicuous because of their large size and basophilic affinity.

One system of lymphatic channels began as minute blind-ending vessels in close contact with Bowman's capsules. No lymphatic vessels were seen round the afferent or efferent arterioles of the glomeruli and none appeared to penetrate through Bowman's capsule. The interlobular capillaries were also free from any lymphatic network. The small lymphatic vessels beginning near Bowman's capsules gradually enlarged and formed nets round both the arterial and venous vessels of the cortex. Particularly dense networks were observed round the large thin-walled venous channels or "sinuses" lying in the outer half of the cortex. These lymphatic vessels round the blood vessels followed successively the interlobular, arcuate, and interlobar arteries and veins, leaving the kidney at the hilus to terminate in the nodes on either side of the aorta. Small blind-ending lymphatic capillaries also originated beneath the mucosa of the papilla, ascended in more or less straight lines through the medulla, and emptied into the larger lymphatic channels round the arcuate arteries and veins. The lymphatic trunks round the arcuate vessels therefore receive lymph from both medulla and cortex.

The author points out the probable function of the renal lymphatic system in regulating the amount of fluid excreted and preventing accumulation of fluid in the kidney. It is known that an increased renal blood flow, in addition to augmenting urinary output, increases the volume of lymph flowing from the kidney. The dense networks of lymphatic vessels observed round the large

thin-walled veins in the outer half of the cortex suggest that the exchange of fluid connected with renal excretion may take place in this region. *R. P. Foggie*

2782. **The Volume of Cell Nuclei in Amputation Neuromas and in Neurofibromas**
R. ALTSCHUL and A. M. FRIESEN. *Cancer Research* [*Cancer Res.*] **9**, 225–227, April, 1949. 13 refs.

2783. **Nodular Hyperplasia of Thyroid Glands Induced by Thiouracil**
G. L. LAQUEUR. *Cancer Research* [*Cancer Res.*] **9**, 247–255, April, 1949. 8 figs., bibliography.

See also Section Infectious Diseases, Abstract 3023.

CLINICAL PATHOLOGY

2784. **Prothrombin: A Critique of Methods for its Determination and Their Clinical Significance**
B. ALEXANDER, A. DE VRIES, and R. GOLDSTEIN. *New England Journal of Medicine* [*New Engl. J. Med.*] **240**, 403–413, March 17, 1949. 3 figs., 46 refs.

Most of the current techniques for prothrombin estimation are based upon the one-stage method of Quick (*Amer. J. clin. Path.*, 1940, **10**, 222) or the two-stage procedure of Warner, Brinkhous, and Smith (*Amer. J. Physiol.*, 1936, **114**, 667). Often the results obtained by these two methods agree closely, but sometimes there is a considerable difference.

As estimated by the one-stage method an elevated prothrombin time may be due to deficiency of prothrombin, labile factor, or fibrinogen singly or in combination. Other variables influencing the result are the Ac-globulin of Seegers, factor V of Owren, prothrombin A of Quick, and the plasma factor of Fantl and Nance, all of which apparently accelerate the conversion of prothrombin to thrombin, as also does a serum factor recently described [*Blood*, 1949, **4**, 247]. Plasma also contains antithrombin which inactivates thrombin, this action being enhanced by heparin. The prothrombin time is also profoundly affected by the source of the thromboplastin used and the method of its preparation. As a plasma diluent, barium sulphate plasma is the best and most readily available agent.

The two-stage method may give inaccurate results when the plasma prothrombin concentration is low, as little dilution is then required and the danger of antithrombic activity is increased. Theoretically, other circulating coagulants may effect the complete conversion of prothrombin to thrombin, on which the two-stage method depends. It is generally agreed that this method is too laborious for routine use in most clinical laboratories. The authors recommend and describe a technique based upon the one-stage method of Quick as modified by Rosenfield and Tuft (*Amer. J. clin. Path.*, 1947, **17**, 405), in which " difco " thromboplastin extract is used and the results are expressed as the percentage of normal prothrombin activity.

[In Britain, Biggs and Macfarlane have shown that Russell's viper venom and lecithin cannot be used to replace brain thromboplastin, and James found that Quick's method using brain thromboplastin provided a more accurate forecast of possible haemorrhage than the one-stage Russell's viper venom method (*J. clin. Path.*, 1949, **2**, 33 and 45). On the other hand, Mawson seems to prefer a one-stage method using Russell's viper venom and lecithin (*J. Lab. clin. Med.*, 1949, **34**, 458).] *A. W. H. Foxell*

2785. **Thermal Coagulation of Serum Proteins. II. Deficient Coagulation in Cancer and the Iodoacetate Index**
C. HUGGINS, G. M. MILLER, and E. V. JENSEN. *Cancer Research* [*Cancer Res.*] **9**, 177–182, March, 1949. 4 figs., 15 refs.

That the serum proteins in cases of cancer differ from those in normal persons is shown by coagulation tests. Sera from patients with pulmonary tuberculosis and acute severe inflammation resemble those from patients with cancer, but sera from newborn infants, normal pregnant women, and patients with non-pulmonary tuberculosis behave like normal sera. A test was devised in which the concentration of iodoacetate which just prevents coagulation of the serum on heating for 30 minutes at 100° C. is determined. This iodoacetate concentration divided by four times the total serum protein concentration yields the " iodoacetate index ", which was below 9 in 85 consecutive clinically active cases of cancer. The index was " negative " (that is, over 9) in 79 out of 95 cases of disease other than cancer. The index was low in pulmonary tuberculosis, chronic nephritis, lobar pneumonia, and infected hydronephrosis. " The coagulation reaction is not specific as a diagnostic instrument although we have found it to be rather useful. From the practical standpoint, the difficulty is . . . in the false positive reactions ". *E. Boyland*

2786. **Critical Considerations on Acute Malignant Histiocytic Reticulosis or Histio-monocytic Reticulosis.** (Considérations critiques sur la réticulose histiocytaire aiguë à évolution maligne ou réticulose histio-monocytaire)
B. DREYFUS. *Revue d'Hématologie* [*Rev. Hémat.*] **4**, 58–69, 1949. 27 refs.

2787. **A Quantitative Turbidimetric Method for the Determination of Spinal Fluid Protein**
H. N. BOSSAK, A. A. ROSENBERG, and A. HARRIS. *Journal of Venereal Disease Information* [*J. vener. Dis. Inform.*] **30**, 100–103, April, 1949. 5 refs.

2788. **Standard Kline Test of Cerebrospinal Fluid for Syphilis Employing Cardiolipin–Lecithin Antigen**
B. S. KLINE and H. SUESSENGUTH. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **19**, 274–277, March, 1949. 4 figs., 3 refs.

2789. **Effect of Caronamide on Excretion of Phenolsulfonphthalein**
W. P. BOGER and J. W. CROSSON. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **19**, 381–387, April, 1949. 2 figs., 15 refs.

Microbiology

2790. **Filamentous Forms Associated with Newly Isolated Influenza Virus**
C. M. Chu, I. M. Dawson, and W. J. Elford. *Lancet* [*Lancet*] **1**, 602–603, April 9, 1949. 4 figs., 4 refs.

Most electron micrographs of influenza virus show round or oval bodies approximately 90 and 100 mμ in diameter, and the preparations studied have usually been purified by differential centrifugation, a process which tends to select particles of a narrow range of size.

The authors demonstrated a much wider variation in the form of influenza virus by making preparations in a different way. Influenza virus was added to saponin-lysed fowl erythrocytes and adsorbed on to the cell membrane. This preparation was then fixed in osmic acid, mounted on a collodion film, and photographed direct or after shadowing. Influenza virus particles were studded all over the cell membrane. The predominating form in the classical A (PR8) and B (Lee) strains was the elementary body, but occasional rod-like structures were seen. When fresh strains from the European epidemic of the winter 1948–9 were examined large numbers of filamentous structures about 100 mμ across and up to several μ in length were seen. Internal structures were evident in some. Shorter rods and elementary bodies were also seen. Twelve recent strains of influenza A virus from different countries showed these forms in early egg passages, with slight variations in the length of the filaments and in the proportion of long to short forms. The filaments appeared constantly and only in virus-infected allantoic fluids and were adsorbed on to and eluted from erythrocytes. Heated virus showed the same structure and homologous immune sera removed both long and short forms from the cell. The filamentous forms were visible under the dark-ground microscope, and agglutination by homologous, but not heterologous, ferret immune serum was also observed in this way.

In preliminary serological studies the recent influenza A strains were found to be antigenically identical, closely related to strains isolated in Europe and U.S.A. in 1947, and but remotely related to the classical PR8 strain. A strain from Ocean Island in the mid-Pacific, isolated in October, 1948, fell into the same serological group and showed filamentous forms. One 1947 A strain from England contained a small proportion of filamentous forms, but had been through a number of passages in the laboratory. One B strain recently isolated in Czechoslovakia also showed a few long forms.

[The evidence for regarding these filamentous forms as a phase of influenza virus multiplication is very strong. The article is illustrated by beautiful electron micrographs showing the form described.] *Alan P. Goffe*

2791. **Measurement of Aerobic Respiration in *Leptospira icterohaemorrhagiae***
P. B. Marshall. *Journal of Infectious Diseases* [*J. infect. Dis.*] **84**, 150–152, March–April, 1949. 3 refs.

BACTERIA

2792. **Actinomycosis. A Pathologic and Bacteriologic Study of Twenty-one Fatal Cases**
L. A. Weed and A. H. Baggenstoss. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **19**, 201–216, March, 1949. 18 figs., 34 refs.

The authors draw attention to the confusion that exists in the literature of actinomycosis owing to the fact that two organisms, with superficially similar morphological characters but with different biological properties, are each associated with the clinical condition known as actinomycosis. One is the obligate aerobic, sometimes acid-fast *Nocardia* and the other the non-acid-fast, micro-aerophilic or anaerobic *Actinomyces*. The aerobic form is commonly found in association with grasses and soils, but not with the normal animal body. The anaerobic form has not been cultivated from grasses, etc., but has very frequently been cultivated from the gastro-intestinal tract of normal animals. The anaerobic form (*A. bovis*) is associated with tissue lesions of the jaw, lungs, and gastro-intestinal tract, and such infections can reasonably be regarded as having arisen from contamination with the normal flora of the gut of the infected person. On the other hand, infection with the aerobic form would appear to be of exogenous origin.

The authors investigated 35 cases diagnosed as actinomycosis at post-mortem examination and were unable to demonstrate *A. bovis*. in 11 of them, while in 3 others there was considerable doubt. Of the 11 negative cases 2 were highly suggestive of *Nocardia* infection and the organism was obtained in pure culture from one of these. In more than half of the cases in which *A. bovis* was found there was evidence of a mixed infection. The presence of sulphur granules and the general histological picture usually considered characteristic of actinomycosis could be the result of infection by organisms other than *A. bovis*; it is the authors' plea that the diagnosis should be reserved for conditions which are associated with the anaerobic organism known as *Actinomyces bovis*.

H. J. Bensted

2793. **The Influence of Penicillin on Production of Haemolysin by *Clostridium perfringens*, Type A.** (Wpływ penicyliny na wytwarzanie hemolizyn przez laseczki zgorzeli gazowej (*B. perfringens*) typu A)
H. Meisel, I. Rybicka, and P. Meisel. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **4**, 361–364, March 21, 1949.

The influence of penicillin was studied by adding it in varying concentration to a culture medium consisting of beef infusion broth enriched with 1% proteose peptone, 1% glucose, and 0·5% NaCl; the medium was adjusted to *p*H 7 to 8. Cultures of *Clostridium perfringens* were grown anaerobically under a layer of liquid paraffin. The following effects of the antibiotic were recorded. In

high concentrations neither bacterial growth nor toxin production occurred; just below the bacteriostatic level growth was permitted but the toxins produced were weaker than in control medium; small—but still active—doses of penicillin modified the growth of organisms and elevated the haemolysin production above the control values. Strains deprived of the ability to produce haemolysin do not produce it under the influence of penicillin. *J. H. Czekalowski*

2794. **Staphylococci in the Newborn. Their Coagulase Production and Resistance to Penicillin and Streptomycin**
G. MARTYN. *British Medical Journal* [*Brit. med. J.*] **1**, 710–712, April 23, 1949. 7 refs.

This is a report on the incidence of staphylococci in the nasopharynx and stools of normal infants in the first 7 days of life. The various strains—obtained from selected colonies on plate cultures—were tested for coagulase production and also for penicillin and streptomycin sensitivity. The specimens from the nasopharynx were collected on swabs taken through the nose, and faecal specimens were collected on the adult-type throat swab passed, with precautions against skin contamination, into the rectum. Nasal swabs were cultured directly on horse-blood agar plates incubated aerobically at 37° C. The rectal swabs were plated directly on to horse-blood agar and MacConkey's agar and, in addition, into Robertson's meat medium with 10% sodium chloride as a staphylococcal selective medium, for subsequent subculture on to horse-blood agar.

In 36% of cultures made from 130 infants coagulase-positive *Staphylococcus pyogenes* was present in both nasopharynx and faeces of the same individual. Over 50% of the nasopharyngeal and the faecal cultures were penicillin-resistant, and all of these produced penicillinase. Only 4 out of the 99 strains of *Staph. pyogenes* isolated were resistant to streptomycin. Of 47 pairs of strains (pairs of cultures from individuals yielding *Staph. pyogenes* from both nasopharynx and faeces) 37 pairs were similar and 8 were different in their sensitivity to penicillin; 2 other pairs differed in their sensitivity to streptomycin. In none of the nasopharyngeal or faecal cultures of the coagulase-positive staphylococci tested was there any evidence of heterogenicity in penicillin sensitivity.

[The culture results do not show relative incidence of coagulase-positive staphylococci in the various age groups from 0 to 7 days; it would be of interest to know on which day of life the organisms begin to appear. When the author states that rectal swabs were taken with due precautions to prevent skin contamination he presumably means gross skin contamination. The investigation would have been more complete had serological classification and phage-typing of the strains been included.] *H. J. Bensted*

2795. **Studies on Streptomycin. VI. The Effect of Streptomycin on the Metabolism of Multiplying Bacteria**
R. J. HENRY, R. D. HOUSEWRIGHT, and S. BERKMAN. *Journal of Bacteriology* [*J. Bact.*] **57**, 447–451, April, 1949. 11 refs.

2796 (*a*). **Enteritis Necroticans due to *Clostridium welchii* Type F**
J. ZEISSLER and L. RASSFELD-STERNBERG. *British Medical Journal* [*Brit. med. J.*] **1**, 267–269, Feb. 12, 1949. 7 figs., 8 refs.

2796 (*b*). **The Toxins of *Cl. welchii* Type F**
C. L. OAKLEY. *British Medical Journal* [*Brit. med. J.*] **1**, 269–270, Feb. 12, 1949. 4 refs.

2796 (*c*). **Recovery of *Cl. welchii* Type F from Preserved Cultures**
C. DIECKMANN. *British Medical Journal* [*Brit. med. J.*] **1**, 270, Feb. 12, 1949.

2796 (*d*). **Origin of *Cl. welchii* Type F Infection**
E. HAIN. *British Medical Journal* [*Brit. med. J.*] **1**, 271, Feb. 12, 1949.

2796 (*e*). **On the Occurrence of *Cl. welchii* Type F in Normal Stools**
E. HAIN. *British Medical Journal* [*Brit. med. J.*] **1**, 271, Feb. 12, 1949.

The first of this series of papers is concerned with the definition of a new type of *Clostridium welchii* which has been recovered from a number of severe cases, many of which were fatal, of a necrotic inflammatory condition of the bowel wall, particularly in the jejunum. The clinical picture was that of an acute enteritis with vomiting and profuse diarrhoea followed by cyanosis and circulatory collapse. Post-mortem examination showed a diffuse sloughing enteritis with tube-like areas of necrosed mucosa a foot or more in length. Material from such lesions was sent to the authors for bacteriological examination, and from all specimens an organism closely resembling *Cl. welchii* was recovered. It was found that the spores of this organism survived boiling for much longer periods than the recognized types (A, B, C, D, or E) of *Cl. welchii*. The new organism produced traces only of *Cl. welchii* α- and γ-toxins but considerable quantities of β-toxin. Other toxins associated with *Cl. welchii*—δ-, ϵ-, θ-, κ-, or λ-toxins—were not demonstrated in culture filtrates. The lethal properties of culture filtrates were entirely neutralized by sera containing *Cl. welchii* β-antitoxin. Guinea-pigs inoculated intramuscularly with cultures of the new organism showed a spreading, glassy, gelatinous oedema similar to that seen in a *Cl. welchii* type B infection. When the organism was injected into the lumen of the intestine of guinea-pigs a condition was observed which was akin to that seen in dysentery of young lambs and in human cases of necrotic enteritis. Growth of the organism was inhibited by 10 units, but not by 1 unit, of penicillin per ml. and clinically the condition appeared to respond to amino-sulphonamide preparations of the " marfanil " (sulphamylon, *U.S.P.*) type. The organism is considered to be a new type of *Cl. welchii* and it is proposed to name it " type F ".

The second paper describes the demonstration in cultures of *Cl. welchii* type F of small amounts of α- and γ- and large amounts of β-toxin. Sera from patients convalescent from clinical necrotic enteritis were also examined and 3 out of 6 were found to contain measurable amounts of *Cl. welchii* β-antitoxin.

The third paper reports that out of a series of 63 preserved cultures of *Cl. welchii* in Ziessler's collection at Hamburg, 2 were found to have the characters of type F. Both were said to have been isolated from war wounds of German soldiers on the Russian front in 1943.

The report of a human case of *Cl. welchii* type F injection, constituting the fourth paper, points to the infection having arisen from the ingestion of tinned rabbit. *Cl. welchii* type F was recovered from the stools of the patient and from the rabbit meat. The usual method of sterilization during the canning process was apparently insufficient to kill off the very heat-resistant spores. The case reported terminated fatally, but two associated cases were trivial.

The last paper gives a short account of the recovery of *Cl. welchii* type F from the stools of a significant proportion (about one-sixth) of 108 individuals who were not presenting a clinical picture of necrotic enteritis. It would appear that there is considerable variation in the toxogenic properties of different strains of this newly described type of *Cl. welchii*, as a high proportion of the strains recovered from normal stools had a very low toxicity. *H. J. Bensted*

2797. **Bacteriology of Necrotizing Enteritis. I. A New Bacillus in the Bowel of Patients with Necrotizing Enteritis. II. The Toxins of *Bacillus enterotoxicus* (*Clostridium welchii* Type F). III. *Bacillus enterotoxicus* (*Cl. welchii* Type F) in the Strains of *Cl. welchii* in the Zeissler Collection of Anaerobes. IV. *Bacillus enterotoxicus* in a Household. V. *Bacillus enterotoxicus* in the Stools of Normal Persons.** (Zur Bakteriologie der Enteritis necroticans. I. Ein neuer Bazillus im Darminhalt von Kranken mit Enteritis necroticans. II. Die Toxine des *Bacillus enterotoxicus* (*B. welchii* Type F). III. *Bacillus enterotoxicus* (*Bacillus welchii* Type F) unter den Stämmen von *B. welchii* der Zeisslerschen Anaerobensammlung. IV. *Bacillus enterotoxicus* (*B. welchii* Type F) in einem Haushalt. V. *Bacillus enterotoxicus* (*B. welchii* Type F) in den Stühlen normaler Personen)
J. ZEISSLER, L. RASSFELD-STERNBERG, C. L. OAKLEY, C. DIECKMANN, and E. HAIN. *Zentralblatt für Bakteriologie, Parasitenkunde, u. Infektionskrankheiten* (*Abteilung* 1, *Originale*) [*Zbl. Bakt.* (1 *Abt. Orig.*)] **153**, 304–325, April 28, 1949. 14 figs., 17 refs.

This series of papers, recently published in English elsewhere [see Abstract 2796 (*a*)–(*e*)], give an account of the aetiology and bacteriology of necrotizing enteritis, formerly an exceedingly rare condition but becoming comparatively frequent in Germany under the chaotic conditions prevailing there after the surrender.

2798. **The Diagnosis of Klebsiella Pneumonia (Friedlander's Bacillus) from the Gastrointestinal Tract of Normal Healthy Adults**
H. E. LIND and D. ALLAN. *Journal of Bacteriology* [*J. Bact.*] **57**, 159–162, Feb., 1949. 12 refs.

A series of 400 stools from healthy adults were cultured on Endo's medium to determine the frequency of occurrence of *Klebsiella pneumoniae*. Cultural identification was further supported by specific agglutination and capsule-swelling tests. Suspected cultures were also tested for mouse pathogenicity. Culturally-characteristic strains of *K. pneumoniae*, of which 3 were mucoid and 7 were smooth, were isolated from 10 stools; three of the strains were typed serologically.

The resistance of the organism to hydrochloric acid broth and to gastric juice was also determined. At *p*H 1, 2, and 3, both in acid broth and in gastric juice, almost all the bacteria were destroyed in one hour. At *p*H 5 and higher there was no inhibition of growth in acid broth, whereas in fresh normal gastric juice approximately 75% of the organisms failed to survive after 4 hours. *G. Payling Wright*

2799. **An Investigation of the Bactericidal Action and Fish Toxicity of Two Homologous Series of Quaternary Ammonium Compounds**
R. R. RUCKER, H. E. JOHNSON, and E. J. ORDAL. *Journal of Bacteriology* [*J. Bact.*] **57**, 225–234, Feb., 1949. 2 figs., 8 refs.

Crude alkyl-dimethyl-benzyl-ammonium chloride compounds have been used successfully in treating hatchery fish suffering from bacterial gill disease. A study has therefore been made of the relative toxicity, both to fish and to bacteria, of those homologous compounds in which the alkyl group varies from C_8 to C_{18}. The toxicity to fish was determined on 2-inch (5-cm.) blueback salmon (*Oncorhyncus norka*); bactericidal action was studied on *Chondrococcus columnaris*, a myxobacterium known to be pathogenic for fish though not necessarily related to this particular disease. During the tests, an effort was made to reproduce the conditions under which fish are treated in the hatcheries; details of the experimental procedures are given. The toxicity of the compounds both for fish and bacteria increased with the increase in length of the carbon chain of the alkyl group—the former toxicity more rapidly than the latter. With the *n*-octyl compound, the bacteria were killed at ten times greater dilution than the fish, but with the *n*-hexadecyl compound the lethal concentration was the same for both.

Some alkyl-trimethyl-ammonium bromide compounds were also studied; they proved less satisfactory, since their toxicity for fish and bacteria was more nearly the same. *G. Payling Wright*

2800. **Clotting of Human Citrated Plasma by Gram-negative Organisms**
E. M. HARPER and N. S. CONWAY. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **60**, 247–251, April, 1948. 9 refs.

A variety of Gram-negative bacteria has been found to be capable of coagulating citrated plasma. This is done by metabolizing the citrate and thus liberating the free calcium ions required for normal plasma clotting. In oxalated plasma and in much-diluted citrated plasma no coagulation occurs. The nature of the coagulation effected by these organisms is thus basically different from that initiated by the coagulase-positive strains of

Staphylococcus aureus. The two kinds of clotting can be distinguished by the addition of heparin to the citrated plasma; this renders it no longer coagulable by the Gram-negative bacteria, though it can still be clotted by active strains of staphylococci. *G. Payling Wright*

2801. **A Serological Investigation of the Paracolon Group of Organisms**
H. SCHWABACHER. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **61**, 63–74, Jan., 1949. 48 refs.

2802. **Studies on the Mechanism of the Shwartzman Phenomenon**
L. THOMAS and C. A. STETSON. *Journal of Experimental Medicine* [*J. exp. Med.*] **89**, 461–478, May, 1949. 7 figs., 20 refs.

IMMUNITY

2803. **Factors Influencing the Maintenance of Antitoxic Immunity**
M. BARR and A. T. GLENNY. *Lancet* [*Lancet*] **1**, 646–649, April 16, 1949. 1 fig., 8 refs.

Observations on the production of diphtheria antitoxin in guinea-pigs and horses are reported which confirm earlier findings (Barr and Glenny, *Lancet*, 1947, **2**, 647). After the injection into guinea-pigs of two Lf doses of diphtheria alum precipitated toxoid (A.P.T.) at an interval of 4 weeks the usual secondary response was followed by a rapid fall in the blood antitoxin level between the 10th day and the 8th week after the second injection; thereafter there was little further change until the 10th month, when the experiments were concluded. After two injections of 2 Lf doses of formol toxoid at an interval of 4 weeks a similar fall in blood antitoxin level was followed by a delayed response between the 1st and 4th months, the level afterwards falling again. In a third group of guinea-pigs, which were given the same doses of formol toxoid but at an interval of 6 weeks, there was only a slow fall in blood antitoxin level until the 6th month, after which there was a gradual rise. In the experiments, two doses of A.P.T. produced far more antitoxin at the peak of the secondary rise than did two of formol toxoid, but the rate of loss was greater and the delayed response was negligible. Experiments in which horses with basal immunity to diphtheria were given two booster doses, one of A.P.T. and one of formol toxoid, at an interval of 4 months suggested that the rate of loss of antitoxin depended on the order in which the two types of antigen were given, being less when formol toxoid was used for the second injection.

In hyperimmunized horses the blood antitoxin level, after an initial fall, tends to remain constant for 2 or 3 years, sometimes even increasing later; thus active production of antitoxin continues long after stimulation has ceased. After a secondary stimulus antitoxin may be formed so rapidly that in 24 hours 2,880 units are produced for each Lf of antigen administered, or 1 unit every 30 seconds. Theories concerning the mode of antibody-production must take these facts into account. It is suggested that cells (probably lymphocytes), already adapted to produce antitoxic globulin by the original antigenic stimulus, reproduce similar cells as a result of the secondary stimulus.

These experimental results in animals suggest that for lifelong immunity children should be given two doses of A.P.T. to establish basal immunity, followed later by doses of formol toxoid to maintain it. The authors conclude with a plea for long-term investigations, which might conveniently be carried out on students, to test the efficiency of different methods of immunization in man.
D. G. ff. Edward

2804. **P.T.A.P.: the Present Position**
L. B. HOLT and G. BOUSFIELD. *British Medical Journal* [*Brit. med. J.*] **1**, 695–699, April 23, 1949. 1 fig., 7 refs.

The use of a semi-synthetic medium in the production of *Corynebacterium diphtheriae* toxin has resulted in a toxoid of consistently high purity, free from constituents of the broth medium used hitherto and also relatively free from bacterial protein other than toxoid. This purified toxoid is adsorbed to aluminium phosphate instead of to alum as in A.P.T. The new product has been labelled P.T.A.P. (purified toxoid precipitated by aluminium phosphate).

Although it has been recognized lately that batches of A.P.T. may differ in their efficacy, successive batches of P.T.A.P. have been found to provide a uniform antigenic stimulus. Thus the Schick conversion rate varied from 94·1% to 100% with P.T.A.P. while for A.P.T. the figures were 85·7% and 97·5%. The authors point out, however, that the differences are statistically not significant. Evidence is produced that response to intramuscular injection of the prophylactic is greater than to subcutaneous administration. The optimal amount of aluminium phosphate per ml. is approximately 10 mg.

Although the toxoid content per dose, as prescribed by law, is 50 Lf per ml., equally good results are obtained consistently with amounts of toxoid as low as 10 Lf per ml., only 6% of cases failing to become Schick-negative after one inoculation with 10 to 30 Lf per ml. Most of the local irritation from the injection can be eliminated by adjusting the *p*H of the prophylactic from 5 to 6·5, without loss of antigenicity. An accurate description of the optimal composition of the prophylactic is given.

[In a leading article on page 715 of the same journal the position of diphtheria prophylactics in general is surveyed and it is pointed out that purified toxoid induces a high antitoxic immunity without necessarily stimulating immune body production against other bacterial proteins probably present in the older and well tried prophylactics. These " incidental " antibacterial antibodies may well play some part in raising the immunity level of a population. The author of this leading article therefore urges extensive large-scale comparative trials of A.P.T. and P.T.A.P. over long periods.]
K. S. Zinnemann

2805. **Titration of Physiologic and Immune Antibodies with Washed and Unwashed Erythrocytes**
J. GUREVITCH, Z. POLISHUK, and D. HERMONI. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **19**, 265–268, March, 1949. 6 refs.

Paediatrics

2806. **The Secretory Rhythm in the Human Breast.** (El ritmo secretor de la mama en la mujer)
E. JASO. *Revista Española de Pediatria* [*Rev. esp. Pediat.*] **5**, 364–372, May–June, 1949. 9 figs., 2 refs.

The breast secretion seems to vary both in quantity and quality according to the needs of the infant. Feeding of infants is carried out according to rules which have been developed over a long period, that is, by regular application to the breast during the day, with a rest at night which varies in length according to the age and needs of the child. It may be, however, that the breast has developed a rhythm like that of the stomach or kidney through the passage of time. An attempt is made to find support for this view in the present work, the factors which may influence the rhythmic secretion of the breast being also studied. The women studied [number not mentioned] were of the middle class, feeding their infants at the breast either entirely or with supplementary bottle feeds. Observations were made in each case for 70 days of the feeds throughout the 24 hours, the quantity secreted per hour being calculated as the percentage of the daily total. Most of the milk was secreted in the hours between 7 a.m. and 10 p.m., the maximum flow being at about 11 a.m. to noon. The smallest percentages were secreted between 11 p.m. and 6 a.m., the least at 3 a.m. The greater the daily quantity secreted (over 500 ml.) the higher the value for the 8 to 9 a.m. period, whereas if 500 ml. was not exceeded 3 to 10 p.m. was the period of greatest secretion. The greater the daily output the greater was the difference between the amounts secreted by day and by night. The length of the nightly rest was also found to cause variations in the rhythm. If no feed was given for more than 8 hours, the most milk was secreted in the morning, the amount dwindling towards evening. With less than 6 hours respite from feeds the daily maximum was achieved between 5 and 6 p.m. The spacing of feeds did not alter the general shape of the curve, but it was noted that with 4-hourly feeds the rhythm was more regular than with 3-hourly ones. The daily rhythm was different for each of the first 3 months of lactation. In the first month there was oscillation and in the second a tendency to " morning rhythm ", with a high morning output. In the third month the " evening rhythm " was established.

The author states that the most regular flow of milk is obtained with 4-hourly feeds and an 8-hour rest at night. He deduces that the secretion is naturally damped down at night, and also that the reason why the first feed is the largest is that the night's secretion is added to what remains in the breast. [The findings confirm those of previous workers, but the author draws a large number of conclusions from inadequate data, and without weighing the pros and cons sufficiently.] *J. G. Jamieson*

See also Section Microbiology, Abstract 2794.

2807. **Nicotinic Acid Tolerance Test in Infants.** (Nikotinsav terhelési próba csecsemőkön)
P. VÉGHELYI and E. SASS-KORTSÁK. *Orvosi Hetilap* [*Orv. Hetil.*] **90**, 249–251, April 17, 1949. 5 refs.

The nicotinic acid tolerance test suggested by Erdei was performed on 25 healthy infants and on 154 infants suffering from different forms of severe illness. The initial dose, 25 mg. for children weighing 5 kg. or 50 mg. for those weighing more, was given in a teaspoonful of water after meals. If no effect was observed, that is, no sudden reddening of the body surface occurred, a further 25 mg. was given every 10 minutes until the characteristic vasodilatation appeared. The reaction was sudden and very definite in all cases. The normal value for the test, expressed as the dose in mg. per kg. body weight, was found in the 25 control cases to lie between 8 and 15.

In 28 of the cases tested values were over 20. All these patients were suffering from severe infections, such as mastoiditis, bronchiectasis, and empyema. Acute infections were associated with the highest values. In one case the value was 44. It was further found that if the child's condition did not improve a high value was maintained for several days or even weeks. In a second group the values lay between 15 and 20. Most of the infants in this group suffered from upper respiratory infections, pyuria, and otitis. Improvement in the infant's condition was followed by a fall in the value, but normal figures of 8 to 15 were not reached for a period varying from 1 to 3 weeks after recovery, that is, after the appetite became normal and body weight began to increase.

The biochemical basis of the reaction is not quite clear. Aminization of nicotinic acid does not take place solely in the liver (as was originally thought by Erdei). However, in all cases of severe infection with some increase in protein catabolism high values for this test were obtained. This also occurs after surgical operations. *S. Sacher*

2808. **Procaine Penicillin in Infants and Children**
W. M. WILSON, J. W. FARQUHAR, and I. C. LEWIS. *Lancet* [*Lancet*], **1**, 866–868, May 21, 1949. 3 figs., 18 refs.

The preparation used was a suspension of procaine penicillin G in arachis oil which, when shaken, readily passed through a 19-gauge needle. Ten patients were selected from each of the following groups: (1) premature infants; (2) infants aged 1 to 5 days; (3) infants aged 7 to 15 days; (4) children aged 1 to 12 months; (5) children of 1½ to 3 years; and (6) children 4 to 9 years old. Groups 1 to 3 were all healthy; groups 4 to 6 were mainly convalescent from acute infections such as meningococcal meningitis, pneumonia, and nephritis. The dose of penicillin, given in a single injection, varied

from 60,000 to 300,000 units according to age. In the infants in groups 1 and 3 a bacteriostatic level was maintained for about 36 hours, but in the second group penicillin was still detectable in the blood of 7 out of 10 babies after 48 hours. The difference was presumed to be due to the period of physiological dehydration following birth. In groups 4 to 6 a therapeutic blood penicillin level was present in 23 out of 29 children at the end of 24 hours. Though penicillin and sulphonamides are used together much more commonly in children than in adults, it was considered inadvisable to advocate this combined therapy until more is known about the possible antagonism between procaine and the sulphonamides.

R. Wien

2809. **The Evaluation of the Combined Effect of Potassium and Adrenal Cortical Extract in Infants with Atrophy and " Toxicosis ".** (Kalium és mellékvesekéreg együttes gyógyhatásának értékelése atrophiás és toxicosisos csecsemöknél)

L. BARTA. *Orvosi Hetilap* [*Orv. Hetil.*] **90**, 119–120, Feb. 20, 1949. 3 refs.

Desoxycorticosterone acetate (DOCA), in doses of 5 mg. daily for 4 to 5 days, with potassium, 150 to 200 ml. daily of a solution containing potassium chloride 0·3 g., sodium chloride 0·5 g., and glucose 10 g. in 100 ml. water, was given to infants with constitutional atrophy and with toxicosis due to dehydration from alimentary causes, and to normal newborn and premature infants.

The author had earlier recorded the observation (*Ann. Paed.*, 1948, **117**, 158) that DOCA restores glycogen metabolism to normal in atrophic infants; since glycogen storage is connected with fixation of potassium, he tries to show that DOCA does not disturb potassium metabolism. This he maintains in spite of Darrow's (*Bull. N.Y. Acad. Med.*, 1948, **24**, 147) observation that DOCA caused loss of cellular potassium through retention of sodium.

Three series of observations were made. (1) The potassium level in blood was found to be raised 1 hour after ingestion of a dose of glucose and lowered 1 hour after a second dose, but not to the initial level; this happened in 6 atrophic infants, but in 2 severe cases the second effect was absent and this was considered to be due to reduced ability of the liver to store glycogen and consequent reduced utilization of potassium; administration of DOCA would correct this defect. (2) The effect of sugar and DOCA on kidney filtration and re-absorption of potassium was observed; glucose increased tubular re-absorption and DOCA did not increase excretion of potassium. The author concludes that when sugar is administered potassium should also be given, and, if liver glycogen metabolism is disturbed, DOCA in addition. (3) Eighty infants were given potassium in the hope of preventing a physiological fall in birth weight; in most cases there was no loss of weight and a gain from the third day; icterus was less marked. Calcium was given intramuscularly at the same time in order to avoid tetany. DOCA would not prevent the fall in weight, but in premature infants, with defective liver glycogen storage, DOCA is said to be of value. [No records of this work are given, and there is no indication that the treatment was tried in controls.]

Dushanka Wolstenholme

2810. **Pinworm Infection and Childhood Behaviour**

E. DENHOFF and M. W. LAUFER. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **77**, 746–752, June, 1949. 12 refs.

In an attempt to discover any relationship between infection with pin-worms (threadworms) and behaviour symptoms 40 children between the ages of 4 and 12 years, patients in a children's psychiatric hospital in Rhode Island, were studied, 28 being infected and 12 uninfected controls. None of the infected children had peri-anal symptoms (pruritus, cutaneous lesions, vaginitis), abdominal pain, nausea, or vomiting—symptoms previously regarded as significant by other observers. The incidence of underweight was high, as was that of enuresis. Anorexia, hyperactivity, masturbation, and nail-biting were common, but statistical analysis showed that there was no significant relation between these symptoms and threadworm infection. Treatment of the infection had no effect on the symptoms; in fact, only 21% of the treated cases showed improvement, whereas 28% of the untreated children improved. The treatment of threadworm infection has consequently been abandoned in the hospital. [This is a further confirmation of the view, now generally accepted, that threadworms give rise to no symptoms in children. Nevertheless the conclusions drawn from observations on a small number of abnormal children should be accepted with reserve.]

J. Vernon Braithwaite

2811. **Streptomycin in the Treatment of Salmonella Enteritis in Infants**

S. ROSS, F. G. BURKE, E. C. RICE, H. BISCHOFF, and J. A. WASHINGTON. *New England Journal of Medicine* [*New Engl. J. Med.*] **240**, 602–603, April 14, 1949. 4 refs.

The authors report on the treatment with streptomycin of 8 cases of salmonella enteritis in infants. Previous reports on the subject have been conflicting, some authors having reported sterilization of the bowel by streptomycin, while others have recorded bacteriological relapse when the drug was discontinued. The ages of the patients in the present series ranged from 8 months to 3 years. The types of Salmonella isolated were: *Salm. typhi-murium* (3 cases), *Salm. oranienberg* (2 cases), *Salm. muenchen*, *Salm. manhattan*, and *Salm. anatis* (1 case each). Rectal swabs were taken daily and three media used for culture: salmonella-shigella agar, desoxycholate-citrate agar, and Kauffman's tetrathionate broth; this last proved to be the most sensitive medium of the three.

The dosage of streptomycin employed ranged from 0·8 to 4·8 g. daily, with an average of 2·4 g. daily, and the drug was given for 8 to 15 days, averaging 11·8 days per patient. Each patient received, on average, a total of 28 g. orally. In 5 cases streptomycin was given intramuscularly in doses of 0·4 to 0·6 g. daily. In only one

case was there bacteriological cure; in 6 other cases there was an inhibitory effect during administration of the drug followed by relapse after treatment was discontinued. In one case—a *Salm. manhattan* infection—the stools were positive throughout and after treatment, although the patient was taking 4·6 g. of streptomycin a day orally. All the patients recovered, but the favourable outcome is not attributed to streptomycin. The streptomycin sensitivity of the organisms ranged from 4 to 12·5 μg. per ml. before treatment and no resistance developed in any case. The authors found that with a dosage of 0·2 to 0·4 g. of streptomycin daily the stool streptomycin content in infants ranged from 10,000 to 20,000 μg. per g. of dried faeces. Thus, they point out, the sensitivity of the organisms in their 8 cases was exceeded 1,000–5,000 times and yet streptomycin therapy was a failure. *William Hughes*

2812. **Some Etiological Factors in the Coeliac Syndrome**
A. BROWN. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **24**, 99–106, June, 1949. 4 figs., 18 refs.

Many theories of the causation of the coeliac syndrome are reviewed in this paper [but the recent suggestion that starch absorption rather than fat absorption is faulty is omitted.] Stress is laid on infection as a possible primary aetiological factor, a condition similar to the coeliac syndrome having been produced in young rats on a diet of high fat value by the administration of 100 mg. of iodoacetic acid daily in the food and 0·5 ml. of streptococcus toxin daily by injection. *W. G. Wyllie*

2813. **Arobon in the Treatment of Infantile Gastroenteritis: A Clinical Trial**
D. BEYDON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **24**, 41–44, March, 1949. 9 refs.

2814. **Staphylococcal Pneumonia in Childhood**
N. G. B. MCLETCHIE. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **60**, 352–356, April, 1949. 7 refs.

The author describes in detail 2 rapidly fatal cases of staphylococcal pneumonia, in infants 2 days and 3 days old respectively, in the nursery of a small rural hospital in Saskatchewan. Both infants were healthy at birth and both appeared to be perfectly normal less than 4 hours before death. The mothers occupied a two-bed private room in the hospital. There was no obvious source of infection. Post-mortem examination in each case showed the entire bronchial tree to be healthy. The lungs showed congestion, patchy collapse, and oedema—common findings in infants dying from various causes—but a diagnosis of pneumonia was suggested by the unusual degree of " toughness " of the lungs and by the presence in one case of widespread small foci of pulmonary necrosis. Swabs taken of bronchial fluid and of lung substance yielded on culture a heavy pure growth of staphylococci. In each case the organism was heavily pigmented, strongly haemolytic, coagulase-positive, insensitive to penicillin, and as sensitive to streptomycin as the standard Oxford staphylococcus.

These 2 cases appear to be the most rapidly fatal of their kind yet recorded. The author reviews the figures for staphylococcal pneumonia at the Regina General Hospital for the past 10 years and concludes that it is the only bacterial pneumonia commonly causing death in the young, that in the newborn it is usually rapidly fatal, that the mortality declines sharply after the first year, and that the type of lung lesion depends on the duration of the disease rather than on the age of the child. The difficulties of treatment in a fulminating infection by a penicillin-resistant organism with such highly invasive and toxic potentialities are discussed, and a plea is made for bacteriological investigation to exclude staphylococcal infection as a possible cause of mysterious epidemics among infants in institutions.

[Although it is pointed out that attempts to trace the source of the staphylococcus in these cases have usually been unsuccessful, some mention might have been made of nasal, throat, and skin swabs being taken from the mothers, the attendants, and the visiting doctor who saw one of the infants 7 hours before death.]
J. M. Alexander

2815. **Results of Treatment by Exsanguination-transfusion of 160 Cases of Haemolytic Disease of the Newborn.** (Résultats du traitement par exsanguino-transfusion de 160 nouveau-nés atteints de la maladie hémolytique du nouveau-né)
J. J. VAN LOGHEM and H. L. J. M. BARTELS. *Revue d'Hématologie* [*Rev. Hémat.*] **4**, 36–40, 1949. 12 refs.

This is a report of the results of exsanguination-transfusion performed in 60 cases of haemolytic disease of the newborn in Holland during the last 2 years. In most cases the umbilical vein technique of Diamond (*Pediatrics*, 1948, **2**, 520) was employed and 500 ml. of blood transfused, giving an estimated replacement of 80%. A rubber catheter, regularly cleaned out with heparin, was preferred to a plastic one. The mortality in this series was 22·5%. As controls, previous children born to the same parents were investigated and it was concluded that among the cases of icterus gravis there had been a mortality of 63·5% before exsanguination-transfusion was introduced. The causes of death in the 36 fatal cases are tabulated and discussed. Kernicterus was the commonest single cause and there was no evidence that the incidence or severity of this complication had been reduced by exsanguination-transfusion. [The criteria by which cases were selected for treatment are given only in very general terms.] *P. C. Reynell*

See also Section Disorders of the Blood, Abstract 2870.

2816. **The Effect of Milk Supplements on the Growth of Children with Nutritive Failure. The Wetzel Grid Findings**
T. D. SPIES and S. DREIZEN. *Journal of Pediatrics* [*J. Pediat.*] **34**, 393–413, April, 1949. 8 figs., 10 refs.

2817. **Antihistaminic Drugs in Pediatric Allergy**
L. H. CRIEP and T. AARON. *Journal of Pediatrics* [*J. Pediat.*] **34**, 414–420, April, 1949. 3 refs.

Medicine: General

2818. **Effect on Marksmanship of Some Motion Sickness Preparations Containing Barbiturates and Hyoscine**
D. B. TYLER. *Journal of Applied Physiology* [*J. appl. Physiol.*] **1**, 737–742, April, 1949. 8 refs.

Tests were made on a company of marines who had just completed a course of training as riflemen. Each man fired the regulation course on two different days. Two hours before firing started each man received two capsules. On the first day all the capsules contained lactose. On the second day the men were assigned at random to one of three groups; each group received a different capsule containing "RCN" (nicotinic acid 100 mg., hyoscine 0·15 mg., and hyoscyamine 0·4 mg. per capsule), or "MSP" ("amytal" 65 mg. hyoscine 0·2 mg., and atropine 0·15 mg. per capsule), or lactose. The results are given in a table. In another experiment two capsules containing "V-12" (ethyl-β-methylallyl thiobarbituric acid, 130 mg. per capsule) were given to each subject in a group of expert riflemen before a test of rapid firing; another group of experts received capsules containing lactose. These results are also tabulated.

None of the drugs had an adverse effect on marksmanship; hence, they can safely be given to military personnel. MSP had a significantly beneficial effect ($P=0·004$) which may be due to the amytal. This suggests that under conditions of stress it may be more desirable to administer a sedative than a stimulant. The doses used were those recommended for preventing motion sickness.

Pamela Holton

2819. **Systematized Amyloidosis.** (Amyloidose systématisée)
J. GATE, J. COUDERT, R. VACHON, and J. COTTE. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **9**, 176–180, March-April, 1949. 3 figs., 7 refs.

2820. **Modification of Biologic Response in Experimental Hypersensitivity**
G. J. DAMMIN and S. C. BUKANTZ. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **139**, 358–362, Feb. 5, 1949. 58 refs.

The authors review the literature on animal experiments designed to find a means of preventing development of the lesions of hypersensitivity. Salicylates, numerous antihistaminic drugs, anticoagulants, and agents with specific toxic actions, such as colchicine and the nitrogen mustards, have been used in such studies with contradictory results. The present authors first studied the effect of intravenous administration of histamine, to determine whether vascular lesions similar to those of experimental hypersensitivity could be so produced. In a series of 11 rabbits receiving daily intravenous injections of 0·1 mg. of histamine base per kg. body weight for periods ranging from 1 to 62 days no such lesions were produced. Secondly, the authors studied the antigen-antibody mechanisms in rabbits after administration of horse serum or bovine globulin. They then subjected one group of animals to simultaneous treatment with horse serum or bovine globulin and with antihistaminic drugs. The authors did not observe any demonstrable effect of the antihistaminic drug on antibody production, antigen-antibody combination *in vitro*, or the development of the Arthus reaction. Heparin was also without effect on the development of the Arthus reaction in rabbits sensitive to horse serum.

In contrast to these negative results the authors report striking observations when nitrogen mustard was used to interfere with the phenomena of sensitization. Five rabbits were initially given intravenous injections of 0·5 mg. per kg. body weight of the bis compound each 4th day, to a total of seven injections. On the 2nd day after the third injection each rabbit received intravenously 10 ml. of horse serum per kg. body weight. The same amount of horse serum was given to each of 5 rabbits constituting a control group. In all rabbits receiving nitrogen mustard a tendency to bleeding and pronounced leucopenia developed. None of the rabbits treated with nitrogen mustard had endocardial or arterial lesions, but 4 of the 5 controls did. None of the rabbits treated with nitrogen mustard had antibody in the circulation on the 7th day after serum injection whereas the controls did. The immediate Arthus reaction, elicited by intradermal injection of 0·2 ml. of horse serum diluted 1 to 1, 1 to 5, 1 to 10, 1 to 20, and 1 to 40, was the same in both groups, but after 24 hours only the rabbits in the untreated group showed haemorrhagic Arthus reactions.

Kate Maunsell

2821. **Propeptan Therapy for Gastro-intestinal Food Hypersensitivy**
A. H. PRICE, F. URBACH, H. A. O'NEILL, and E. J. TALLANT. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **16**, 161–171, May, 1949. 2 figs., 45 refs.

Propeptanes are predigested individual proteins which consist of proteoses, peptones, subpeptones, simple peptides, and amino-acids. For the purpose of desensitization the food to which the patient is hypersensitive is eliminated from the diet and the relevant propeptane is administered in capsule form 45 minutes before each meal. After 3 days, in the absence of symptoms, the offending food is added to the diet in gradually increasing amounts. Ten patients with various food allergies were so treated. The *x*-ray appearance of the small intestine was investigated under the influence of the incriminated food before and after treatment. Hypersensitivity shows itself by narrowing of the bowel to less than 1·5 cm. calibre; segmentation, manifested by loss of continuity of the barium column; and scattering, shown by retention of some scattered barium in the ileum after the column has

passed. Most of these abnormal radiological appearances were absent after treatment was completed, and the clinical improvement in 7 patients is described as excellent; in 3 others, in whom psychiatric disorders were also present, improvement was temporary. *H. Herxheimer*

2822. **Oral Pollen Absorption. Demonstrated by Controlled Passive Transfer Tests**
T. M. FEINBLATT and R. LOVE. *Annals of Allergy* [*Ann. Allergy*] 7, 228–231, March–April, 1949. 7 refs.

Administration of dry pollen by mouth (in the form of three capsules, each containing 30 mg.) to 52 control subjects not sensitive to pollens caused in 21 a reaction at skin sites previously rendered passively sensitive with serum from pollen-sensitive donors. The reactions were compared with those at similarly prepared skin sites after subcutaneous injection of 1,000 pollen units of Lederle mixed antigen into the deltoid region. Positive reactions of similar size, with a maximal effect in the same average time of 2·6 hours after administration, occurred in 20 of the 52 subjects. In 13 subjects reactions were obtained when pollen was given by mouth or parenterally; in 12 a reaction developed after administration of the pollen by one route or the other, but not by both. [There were wide individual variations in the time taken for a maximal reaction to develop. There was no constant relation between the maximal response after oral administration and that after parenteral injection in subjects who reacted to both.] *R. S. Bruce Pearson*

2823. **The Role of Streptococci in Bronchial Asthma. Etiologic Significance and Treatment with Streptococcus Filtrates**
H. A. HEISE. *Annals of Allergy* [*Ann. Allergy*] 7, 240–249 and 257, March–April, 1949. 3 figs., 9 refs.

The author believes that asthma is often the result of antigen-antibody mechanisms evoked by the products of long-chain α-haemolytic streptococci which are themselves not toxic. These conclusions are based on the effects of treatment of 328 asthmatics with a filtrate prepared from such streptococci. Patients whose asthma appeared to be caused solely by inhalant sensitivity were excluded from this series. The organisms from which the filtrate was prepared were isolated from sputum of asthmatic patients, cultured on " bacto-brain veal agar ", and subcultured in deep " bacto-nutrient broth ", to which had been added 0·5% of sodium chloride and of dextrose, several small pieces of calf brain, and marble chips. After 4 days' growth, the broth was filtered through a Seitz filter, tested for sterility and used in a dilution of 1 in 1,000,000 made up with buffered saline. This filtrate contained a bacterial product which was destroyed by boiling, as shown by its subsequent failure to provoke skin reactions. Injection of the unboiled filtrate into sensitive subjects caused severe asthma unless it was used in high dilution. In controls injection of 0·5 ml. of the undiluted filtrate caused only slight local reactions.

An initial dose (usually 0·02 ml. of 1 in 1,000,000 dilution), unlikely to cause a focal reaction, was selected. This was injected intradermally, was usually doubled in successive doses, and given at first daily, but later with gradually increasing intervals up to a month or more. Improvement often began within a few days of starting treatment, but relapses after completion of the course were not uncommon.

Of the 328 cases of intrinsic asthma treated by this method improvement or complete relief occurred in 90% of those under 20 years of age, and in 70% of those above this age. In those patients also sensitive to pollens it was observed that symptoms recurred when the pollen season came round, though there had been no attacks during the winter months. *R. S. Bruce Pearson*

2824. **The Nature of Benadryl Activity and its Clinical Applications**
T. H. MCGAVACK. *Annals of Allergy* [*Ann. Allergy*] 7, 232–239, March–April, 1949. 17 refs.

" Benadryl " was shown to have the following effects in healthy human subjects: (1) The wheal and flare caused by local introduction of histamine was prevented by topical application of an ointment (2·5%), or by daily ingestion of 300 mg. by mouth for a period of 3 weeks. Intravenous injection of 10 mg. had no effect on the skin response to histamine when the latter was tested subsequently at hourly intervals for 4 hours. (2) The free acid and total acid secretion of the stomach fell appreciably in most cases after 3 weeks' treatment with 150 to 400 mg. of benadryl daily. (3) A slight fall in blood pressure occurred in some cases after a daily dose of 300 mg. for 3 weeks. The pulse rate was not affected. (4) Mydriasis occurred in 75% of cases after the use of eye drops containing 0·5% benadryl. (5) Capillary permeability was reduced in 7 out of 11 patients receiving a daily dose of 150 mg. or more for 3 weeks. (6) Glucose tolerance was increased after a single intravenous dose of 30 mg. A single oral dose of 400 mg. had no effect.

Side effects occurred in 131 of 242 patients treated for various diseases and included drowsiness (27·6%), dryness of mouth (17·6%), dizziness (14·2%), weakness (9·5%), incoordination and light-headedness (2·9%), blurring of vision (2·7%), and loss of memory (0·8%).

The author concludes that benadryl directly blocks the effect of histamine in the tissues and has a hyoscine-like action on the sensorium. These two actions vary in different individuals. The dosage must be adapted to both the individual and the disease. The initial dose is usually 150 mg. daily in three doses of 50 mg. If 250 mg. is necessary, five 50 mg. tablets are given, two of them being taken at bed-time. If more than 400 mg. is required, 50 mg. given 2-hourly is found to be most effective. Where rapid action is desired as in Ménière's syndrome, migraine, or angioneurotic oedema, 30 mg. in aqueous solution can be given intravenously. An ointment (2%) is most useful in itching dermatoses. The largest doses of the drug are required in extensive conditions such as urticaria, neurodermatitis, and asthma. The daily dose can be cautiously reduced when a satisfactory result has been obtained. Side effects tend to diminish with continued use of the drug.
R. S. Bruce Pearson

2825. **The Effect of Substitution of Antistine (Phenyl-benzyl-amino-methyl-imidazoline) for Benadryl or Pyribenzamine during the Height of the Ragweed Pollen Season**
B. DICKSTEIN. *Annals of Allergy* [*Ann. Allergy*] **7**, 250–253, March–April, 1949. 4 figs., 7 refs.

The relative efficacy of "benadryl", "pyribenzamine", and "antistine" was assessed in 17 cases of ragweed sensitivity. Antistine 100 to 200 mg. was substituted for benadryl (25 to 50 mg.) or pyribenzamine (25 to 50 mg.) which in every case had controlled the patients' symptoms satisfactorily. Only 8 patients continued to experience relief with antistine; 9 relapsed. Pyribenzamine was found to be the most (100%), benadryl the next (76%), and antistine the least effective (47%). Antistine caused fewest side reactions, pyribenzamine the most. *R. S. Bruce Pearson*

2826. **Benadryl: Intravenous use in Allergy**
B. ZOLOV. *Annals of Allergy* [*Ann. Allergy*] **7**, 254–257, March–April, 1949. 4 refs.

"Benadryl" (10 mg. per ml.) diluted in 2 ml. of saline was given intravenously to 26 patients in 10 to 20 mg. doses over a period of 2 minutes. These patients included 14 with bronchial asthma, 4 with hay-fever (ragweed pollenosis), 3 with allergic rhinitis, and 5 with urticate and pruritic skin conditions. In 10 cases there was no improvement, in 10 improvement, and in 7 excellent results. The beneficial effect lasted for 3 to 4 hours. Three patients experienced side effects in the form of nausea (1), severe headache (1), and rigors (1).
R. S. Bruce Pearson

See also Sections Disorders of the Blood, Abstract 2866; Infectious Diseases, Abstract 3037

2827. **Citric Acid in the Blood: its Significance and Changes in Rickets.** (Verhalten und Bedeutung der Blut-Citronensäure bei Rachitis)
T. OCHSÉ. *Annales Paediatrici* [*Ann. paediatr., Basel*] **172**, 139–154, March, 1949. 1 fig., 30 refs.

The solubility of calcium salts in the blood is closely related to the presence of citric acid in a certain concentration. Normally 50% of the calcium in blood is ultrafiltrable. The addition of citric acid increases this figure to nearly 100% by the formation of a calcium-citric acid compound (Hastings complex), which also promotes calcium absorption by preventing excessive excretion of insoluble calcium phosphate from the intestinal tract.

Experimental rickets in animals has been successfully treated by the addition of citric acid to the food. In human rickets, especially in cases resistant to vitamin D, favourable results have been observed after the administration of 8 to 10 g. of sodium citrate daily for 3 to 6 weeks.

The author investigated the citric acid level in blood in various age groups and conditions. Pulcher's method was used, citric acid being converted into pentabromacetone and, after the addition of pyridine, photometrically determined. The accuracy of the results was checked. The level of citric acid in the blood of healthy babies up to one year of age (22 cases) was 1·3 to 3·0 mg. per 100 ml., and in children of 1 to 14 years (11 cases) 1·2 to 2·75 mg. per 100 ml. In adults values of 1·2 to 2 mg. per 100 ml. were found in the blood, 1·4 to 2·8 mg. per 100 ml. in the plasma, and 0·8 to 1·2 mg. per 100 ml. in the erythrocytes (11 cases).

Comparison of these figures with those found in 18 rachitic children revealed in the latter slightly higher values, but the difference amounted only to $1{\cdot}16 \pm 0{\cdot}75$ mg. per 100 ml. The administration of large doses of vitamin D (600,000 i.u.) produced in all cases of rickets a reduction in the citric acid values in the blood during the healing phase (from 1·6 to 4·8 mg. per 100 ml. before the therapy to 0·96 to 3·2 mg. per 100 ml.).

The author considers that citric acid therapy may partly compensate for a vitamin-D deficiency, but that its antirachitic action is not yet proved.
M. Dynski-Klein

2828. **Syndrome of Salt Depletion Induced by a Regimen of Sodium Restriction and Sodium Diuresis**
L. A. SOLOFF and J. ZATUCHNI. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **139**, 1136–1139, April 23, 1949. 14 refs.

The authors give details of 4 patients with congestive cardiac failure who developed signs of renal failure and died after being energetically treated with a salt-poor diet and mercurial diuretics. Further details are given of cases where the syndrome of salt depletion was recognized and corrected, and in which recovery was rapid. Weakness, lassitude, anorexia, nausea, vomiting, restlessness, thirst unrelieved by plain water, apathy, mental confusion, fall in blood pressure, increase in pulse rate, diminution in volume of the pulse, clammy skin, shock, and coma are the symptoms and signs which may result from excessive salt depletion. *Geoffrey McComas*

2829. **Recrystallized Insulin for Diabetic Patients with Insulin Allergy**
J. E. JORPES. *Archives of Internal Medicine* [*Arch. intern. Med.*] **83**, 363–371, April, 1949. 23 refs.

This paper is important and completely solves the therapeutic problem of those extremely rare diabetics who show severe and combined allergic reactions to insulin injections and can hardly tolerate the necessary treatment. Such reactions have, since 1925, become more uncommon as commercial insulins have become purer, but still a minor residuum of allergic patients remains. When insulins recrystallized 2 to 7 times were employed by the authors local and general reactions were abolished. It therefore appears that such patients were sensitive not to the insulin molecule itself but to some attached protein impurity. Such allergy still remains a puzzle, because the majority of patients who required these pure recrystallized products for a time showed no allergy when re-treated with less pure products.
R. D. Lawrence

See also Section Endocrine Disorders, Abstract 2926.

Cardiovascular Disorders

2830. **A Method for Recording the Arterial Pressure Pulse and Blood Pressure in Man**
L. H. PETERSON, R. D. DRIPPS, and G. C. RISMAN. *American Heart Journal* [*Amer. Heart J.*] **37**, 771–782, April 15, 1949. 9 figs., 13 refs.

A description is given of an instrumental arrangement for recording, by direct-writing amplifier oscillograph connected by catheter to the radial artery, blood pressure and pulse pressure waves.

The tracings so obtained in a variety of conditions are discussed. *G. Schoenewald*

2831. **Cardiovascular Rejectees. A Follow-up Study**
P. D. WHITE, R. L. LEVY, W. J. KERR, W. D. STROUD, and G. K. FENN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **139**, 1049–1053, April 16, 1949. 9 refs.

Re-examination in 1943 of 4,994 men previously disqualified by local boards from general military service in the U.S. armed forces because of suspected cardiovascular defects enabled 863 to be regraded as fit for service, 447 of whom were accepted. The chief diagnostic difficulties arising at that time lay in the interpretation and assessment of apical systolic murmurs, the definition of the limits of normal blood pressure, resting pulse rate, and heart size in relation to body build, and evaluation of results of exercise tests and electrocardiographic findings, while there was doubt as to the desirability of rejecting men with a diagnosis of neurocirculatory asthenia, or a history of recent rheumatic fever without evidence of cardiac disease. The present (1947) follow-up study of 303 of those men who had been regraded as 1A in 1943 was carried out in order to assess the effects both of the war and of post-war adjustment on their cardiac condition.

At least 50% still had trivial heart murmurs; 4 had developed rheumatic heart disease since 1943, but in those who gave a history of rheumatic fever in childhood or early life without demonstrable sequelae in 1943, "recurrence of activity between 1943 and 1947 was distinctly uncommon". There were no significant changes in heart size, with the exception of 4 men who had developed definite enlargement, one of whom was hypertensive, the others apparently healthy. Of 67 men with transient hypertension at their first examination, 33 now had normal readings, 17 still showed transient hypertension, and 17 had developed sustained hypertension. Another 10, whose blood pressure was normal in 1943, now had sustained hypertension, and 13 had developed transient hypertension. No conclusions could be drawn from analysis of the pulse rates. The electrocardiogram had become abnormal after 4 years in only one case, and 7 men were thought in 1947 to have neurocirculatory asthenia which had not been diagnosed in 1943. The authors conclude that these 303 men, in general, "served long and well in the Armed Forces", and few were discharged for cardiovascular reasons.
J. L. Lovibond

ELECTROCARDIOGRAPHY

2832. **Glycoside Action on the Electrocardiogram and Myocardium. Third Communication.** (Glykosidwirkung auf Elektrokardiogramm und Myokard. III. Mitteilung)
E. SUTER, E. ROTHLIN, and R. BIRCHER. *Helvetica Physiologica et Pharmacologica Acta* [*Helv. physiol. pharmacol. Acta*] **7**, 1–36, 1949. 9 figs., 31 refs.

In experiments on cats the effect upon the electrocardiogram of repeated small, medium, and large doses of various digitalis glucosides was studied and correlated with clinical observations and histological findings. The following compounds were investigated: K-strophanthosid, digilanid A, digilanid C, and digitoxin. As digitalis intoxication progressed the following electrocardiographic changes were found: lowering of P waves and QRS complexes, elevation of S–T junctions, occasional increase in height of T waves (where these had been lowered, isoelectric, or inverted), increasing bradycardia, lengthening of P–Q and shortening of Q–T, supraventricular and ventricular arrhythmias. These changes are divided into 3 stages: (1) therapeutic stage, with changes in P, PQ, QRS and (sometimes) QT; (2) toxic stage, with ST and T changes and supraventricular disturbances of rhythm; (3) terminal stage, with ventricular ectopic arrhythmias. It is pointed out that the electrocardiographic changes do not give any reliable indication of the degree of digitalis effect, but depend on the response of the individual animal. The toxic stage in the electrocardiogram is associated with deterioration in the general condition and, particularly with loss of weight, which is not necessarily due to vomiting; these clinical changes are as reliable a sign of intoxication as the electrocardiographic changes. The occurrence of heterotopic beats and arrhythmias is a sure sign of toxicity. Attention is drawn specially to the observation that the effect of the glucosides may be periodic; a stage of intoxication may be followed by clinical and electrocardiographic recovery although administration of the drug continues in the same way and dosage. Such periods of intoxication alternating with periods of recovery were observed with digilanid A and C, and with digitoxin, but not with K-strophanthosid. Histological changes were constantly found in connexion with large doses of the glucosides. With medium and small doses no constant relation between histological and electrocardiographic changes was found. (See also *Helv. physiol. pharmacol Acta*, 1947, **5**, 298 and 322.)
A. Schott

2833. **High Frequency Cardiodiagraphy with the Usual Electrocardiographic Leads, with Preliminary Remarks on Diagraphy in General.** (Cardiodiagraphie à haute fréquence en dérivations électrocardiographiques usuelles avec des remarques préliminaires sur la diagraphie en général)
E. DONZELOT and J. B. MILOVANOVICH. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **42**, 227–239, Feb., 1949. 12 figs.

A technique is being evolved which is based on the principle that the penetration of high-frequency waves through an organ is modified by changes in the shape, size, or position of that organ. It is stated that details of the method will be published later. High-frequency waves were passed through the chest of human beings and, after condensation and amplification, they were recorded on an electrocardiograph. The authors show that this method may eventually be of value in the study of the various phases of cardiac contraction and that it may allow a separate study of the activity of the left and right ventricles [but the interpretation of their findings is as yet too complex and equivocal to be of value in clinical practice or research]. *E. M. Glaser*

2834. **Practical Aspects of Spatial Vectocardiography with Observations on the Axes of Unipolar Leads and on the Limitations of Einthoven's Hypothesis.** (Aspects pratiques de la vectographie spatiale avec des remarques sur les axes des dérivations unipolaires et l'exposé des limites de l'hypothèse d'Einthoven)
E. DONZELOT and J. B. MILOVANOVICH. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **42**, 352–370, March, 1949. 8 figs., 19 refs.

The authors describe the advantages of their method of vectocardiography, the spatial orientation of the axis in the various leads, and the practical limitations of Einthoven's triangle. The relation between the frontal vectocardiogram and the various limb leads, and that between the horizontal vectocardiogram and the unipolar chest leads, are discussed. Unipolar spatial vectocardiography with the leads Vf, V2 and V6 is briefly described. *A. Schott*

9835. **The Effect on the Precordial Electrocardiogram of Insulating Areas of the Anterior Chest Wall**
A. H. DOUGLAS and J. S. KALTER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **30**, 799–809, April, 1949. 9 figs., 1 ref.

In order to investigate the degree to which areas of the anterior chest wall situated at a distance from the exploring chest electrode may influence precordial electrocardiograms, the anterior chest wall was covered with an insulating wax paper in which holes of 1 in. (2·5 cm.) diameter were cut in positions 1 and 5. A towel saturated in warm saline solution was placed over the wax paper and the exploring electrode was placed in succession in positions 1 to 6 on top of the towel. CF leads were recorded. Only in positions 1 and 5 was the exploring electrode in direct electrical contact with the praecordium. This series of tracings was compared with a control series obtained in the usual way before the application of the wax insulator. In addition, the 3 standard (bipolar) leads and lead III in deep inspiration were recorded. The 25 subjects investigated included normal controls and patients with myocardial infarction, bundle branch block, and right and left ventricular strain. The effects on the electrocardiogram of more remote zones were found to be often more pronounced than is generally assumed, affecting QRS complexes as well as T waves, although the degree varied in different cases. Some apparent discrepancies between leads I and CF_5 could be explained by the interference of more remote areas on the CF_5 pattern. Several representative records are reproduced. *A. Schott*

2836. **A Simple Formula for Clinical Interpretation of the QT Interval.** [In English]
O. LJUNG. *Acta Medica Scandinavica* [*Acta med. scand.*] **134**, 79–86, 1949. 4 figs., 22 refs.

HEART

2837. **Early Recognition of Cardiopulmonary Insufficiency in Pulmonary Emphysema and Sclerosis.** (Раннее распознавание кардио-пульмональной недостаточности при эмфиземе легких и пневмосклерозе)
A. I. GEFTER. Клиническая Медицина [*Klin. Med., Mosk.*] **27**, No. 3, 46–52, March, 1949.

Can the early stages of heart failure be recognized in the presence of pulmonary insufficiency? The author believes that they can, and describes four stages in the development of cor pulmonale: (1) latent pulmonary functional disturbance; (2) established pulmonary insufficiency; (3) pulmonary insufficiency with latent circulatory disturbance; (4) cardio-pulmonary insufficiency. He does not discuss the first, second, and fourth stages, because the first two presuppose the absence of heart failure and the fourth is easily diagnosed.

The third stage is difficult yet important to recognize. The characteristic features of this stage are as follows. (1) Increasing disturbance of respiratory function and increased hypoxaemia, as shown by a falling vital capacity and breath-holding time. (2) Increased difference between the arterial and venous oxygen concentrations. (3) Fall in oxygen concentration of the blood. (4) Slowing of the circulation time, especially at the periphery. This is measured by the fluorescein method of Sorenson, adapted by Votchal. Fluorescein solution is injected into the brachial vein of one arm, and a drop of blood is taken from the brachial artery and vein of the opposite arm every second. The time of appearance of the fluorescein in the arterial blood gives the circulation time in the pulmonary circuit; that of the dye in the venous blood the circulation time in the complete circulation; and the difference that in the peripheral circulation. The prolongation of circulation times in his case averaged 2·2, 6·2, and 4 seconds respectively. (5) Fall in utilization of oxygen by tissues on exertion, whereas in the second stage there is actually an increase under such conditions—from 39 to 45% in his 38 cases. The average

fall in 24 third-stage cases was from 39·2 to 33·7%. (6) The electrocardiographic changes in the third stage consist of a widening of the earlier part of the ventricular complex and elevation of the S–T interval in the right partial electrocardiogram; often a well-marked Q wave and a lowered T wave are present in lead III. (7) Clinically there are progressive cyanosis and dilatation of the jugular veins on pressure over the liver region.

[The " right partial electrocardiogram " referred to is one taken according to the method of Borisova and Rusinov, in which the indifferent electrode is placed on the right arm and the other in the midline of the chest at the level of the ensiform cartilage. The left partial electrocardiogram is taken with electrodes on the left leg and in the left mid-axillary line at the level of the heart's apex. These leads are much employed by Soviet cardiologists.] *L. Firman-Edwards*

2838. **Negative Results of Tocopherol Therapy in Cardiovascular Disease**

C. K. DONEGAN, A. L. MESSER, E. S. ORGAIN, and J. M. RUFFIN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **217**, 294–299, March, 1949. 17 refs.

Three groups of patients were studied: (*a*) 7 with hypertension but with no radiological evidence of cardiac enlargement; (*b*) 7 with hypertension and cardiac enlargement; (*c*) 7 with angina pectoris. All were given tocopherol by mouth in doses ranging from 150 mg. of mixed tocopherols to 600 mg. of α-tocopherol daily for a month at a time alternating with placebos for a month. The patients were studied for from 5 to 20 months. It was shown that the blood level of tocopherol can be significantly raised by oral administration. No appreciable subjective or objective benefit was observed. *C. Bruce Perry*

2839. **Hepatic Pain on Effort. A Test of Right Ventricular Insufficiency.** (L'hépatalgie d'effort. Test d'insuffisance ventriculaire droite)

J. LENÈGRE and A. MATHIVAT. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **65**, 230–243, 1949. 2 figs., 20 refs.

" Hepatic pain on effort " is defined as a dull pain in the hepatic region, which disappears rapidly with rest, experienced as a result of physical effort by patients with cardiac disease. This symptom occurred in 52 out of 128 patients with right ventricular insufficiency, particularly in rheumatic mitral disease and cor pulmonale. Hepatic pain, usually preceded for several months by dyspnoea on exertion, was rarely the presenting symptom of cardiac insufficiency and was occasionally confused with angina of effort. Associated signs included an enlarged pulsating liver, distended jugular veins with increased venous pressure up to 47 cm. of water, and the presence of the hepato-jugular reflux (jugular venous distension lasting more than 30 seconds after hepatic compression). There were also cardiac enlargement and increased right ventricular pressure of 15 to 90 cm. of water. The authors suggest that as a result of effort the increased cardiac debt raises the pulmonary hypertension already present in these patients. This leads to overloading and dilatation of the failing right ventricle, with increased auricular and vena-caval pressures which, transmitted to the liver, cause acute painful congestion. They observe that hepatic pain on effort responds rapidly to treatment directed to correcting the right ventricular insufficiency and consisting of rest, low chloride intake, mercurial diuretics, and digitalis in adequate dosage. *I. Ansell*

See also Section Infectious Diseases, Abstract 3023.

2840. **Incidence of Rheumatic Disease and Subacute Bacterial Endocarditis during the War and the Post-war Period.** (О частоте заболеваемости ревматизмом и подострым септическим эндокардитом в период великой отечественной войны)

Y. G. ETINGER and M. G. SCHMERLING. Терапевтический Архив [*Terap. Arkh.*] **21**, No. 2, 15–23, March– April, 1949. 1 fig., 8 refs.

Study of clinical material and statistical data reveals that the incidence of rheumatic disease considerably diminished in Russia during the late war, whereas during the post-war period there has been a tendency to increase again. The authors also observed a sharp fall in the incidence of the polyarthritic form of rheumatism among adults. In 1940, 3·4% of all patients in their clinic in Moscow were suffering from the polyarthritic type of rheumatism. During the war years on the average 0·25% of all patients had rheumatic polyarthritis, an incidence 14 times less than that in 1940. The lowest figures were obtained in 1944, with an incidence of only 0·1%. During the war there was also a marked decrease in incidence of the cardiac form of rheumatism (non-arthritis type) amongst adults, but the decrease was not so substantial as that of polyarthritis.

Statistics also show that there was a very marked decrease in the incidence of cardiac forms of rheumatism amongst children. The mortality from cardiac affections in children was 10 times lower than in the pre-war period. The incidence of chorea during the war years was only one-tenth of that in the pre-war period. The incidence of subacute bacterial endocarditis during the war did not show any substantial change, but increased almost three-fold during the post-war period.

The reasons for these decreases in incidence are not at all clear. It may be due to a low virulence of the haemolytic streptococcus during the war years, but other causes such as change of diet no doubt played their part. *H. W. Swann*

2841. **Digitalis Bigeminy: An Analysis of Fifty Cases**

E. L. SAGALL and L. WOLFF. *New England Journal of Medicine* [*New Engl. J. Med.*] **240**, 676–680, April 28, 1949. 17 refs.

Electrocardiographic records showing bigeminy were found in 174 cases over a period of 20 years at the Beth Israel Hospital, Boston. In 82 the condition had no relation to digitalis administration and 19 of these patients had no recognizable heart disease. To the

remainder digitalis had been administered and in 50 the abnormality appeared for the first time after full therapeutic doses. Among those given digitalis the commonest accompanying heart disease was rheumatic, while among the others hypertensive and coronary disease were the common associated conditions. In the latter group the ectopic contractions arose more frequently in the left ventricle, while in those given digitalis they were more commonly multifocal and arising in the right ventricle. In many instances bigeminy was the first or only manifestation of digitalis overdosage and it did not accompany other toxic symptoms such as vomiting. It was often persistent for a long time after the drug had been stopped and occasionally seemed to become permanent.

The literature is reviewed and it is pointed out that although irregular extrasystoles occur in digitalis poisoning in the intact mammalian heart and normal man, bigeminy is never produced. Other workers also hold that digitalis alone is not responsible, and that other unknown factors must be present to facilitate its development. The arrhythmia is precipitated more easily in patients with severe heart disease. The seriousness of digitalis bigeminy is difficult to evaluate. Death frequently follows. It is therefore wise to suspend the drug whenever bigeminy is noted. *J. McMichael*

2842. **Cardiac Aneurysm**
M. CAPLAN and P. M. SHERWOOD. *New England Journal of Medicine* [*New Engl. J. Med.*] **240**, 629–637, April 21, 1949. 4 figs., 40 refs.

Before 1931 cardiac aneurysm was diagnosed ante mortem only ten times and the prognosis was considered gloomy. More recently, cases of survival for up to 18 years after diagnosis have been reported, and these patients have lived useful lives. The diagnosis is now no longer rarely made. Two cases are reported, with a review of the literature.

Myocardial infarction due to coronary artery disease accounts for at least 85%, but rheumatic, syphilitic, mycotic, embolic, traumatic, and congenital varieties are recorded. The common site is an anterior one in the area supplied by the left descending coronary artery. Posterior aneurysm has only once been diagnosed ante mortem. Septal aneurysm has never been diagnosed ante mortem, but might be expected to cause Bernheim's syndrome [a doubtful clinical entity]. The condition is associated with replacement fibrosis of the myocardium with adherence of the overlying pericardium; calcification is common (30%). The average size of the aneurysm in 21 specimens was 2 to 4 cm. in diameter by 1·2 to 3 cm. in depth, but during life intracardiac pressure will obviously make the aneurysm larger; more than one aneurysm may be present (6 of 21 cases). In 10% of patients with myocardial infarction a cardiac aneurysm develops. Men are more frequently affected than women. The symptoms are those of the underlying coronary artery disease.

Abnormally large or double cardiac apical impulse, the finding of an irregular cardiac outline on percussion, and a muffled first sound, form a suggestive triad of signs which may be supplemented by apical gallop rhythm and systolic murmur in the area of abnormal pulsation (gallop rhythm may be due to failure of closure of the anterior leaflet of the mitral valve because the anterior papillary muscle pulls upon it when the ventricular wall bulges under systolic pressure). The blood pressure is commonly normal, both before and after the development of aneurysm, and it has been suggested that the hypertrophied myocardium in hypertension is less liable to aneurysm after infarction. There is no typical electrocardiographic pattern, but there may be right axis deviation in an obviously large heart, a low R wave in lead I, and deep S waves in leads II and III. Radiography commonly reveals a bulge in the ventricular wall and paradoxical or absent pulsation of the bulge. Rarely, a thrombus in the sac casts an unduly dense shadow; calcification may occur in the wall or in the thrombus. *x*-Ray kymography is useful, and inflation of the stomach with air is helpful at times. Angiocardiography may help.

Differential diagnosis is from a para-pericardial pad of fat, localized pericardial effusion, metastatic tumour, mediastinal tumour (such as dermoid), aneurysm of the aorta, hydatid cyst, pericardial diverticulum, an enlarged pulmonary conus, and primary myocardial tumour. Prognosis is that of the underlying vasculo-myocardial disease. Rupture is very rare once the acute episode is past. Embolism is not uncommon. The possibly dangerous effects of early ambulation and the possible results of anticoagulant therapy in preventing intramural thrombus and weakening the aneurysm are discussed.
John Anderson

2843. **Right Ventricular Stenosis (Bernheim's Syndrome)**
T. EAST and C. BAIN. *British Heart Journal* [*Brit. Heart J.*] **11**, 145–154, April, 1949. 8 figs., 8 refs.

The authors point out that since Bernheim first described right ventricular stenosis in 1910 very little has been published on the subject, especially in recent years. They add clinical details of a further 5 cases, in 4 of which necropsy was performed. The syndrome consists essentially of what appears to be a clinical paradox, namely, conspicuous features of apparent failure of the right side of the heart in a patient with a lesion on the left side. This is due, as originally pointed out by Bernheim, to the ventricular septum bulging into the cavity of the right ventricle and so preventing its filling. The pulmonary circulation remains unaffected till near the end and orthopnoea does not occur. Hypertension and aortic stenosis, both conditions which produce concentric hypertrophy of the left ventricle, are the lesions giving rise to the syndrome. Three of the present patients had hypertensive heart disease and 2 aortic stenosis. The enlargement of the left ventricle resulting from aortic incompetence does not give rise to the syndrome, presumably because the septum does not become sufficiently thick. Radiologically the right auricle is engorged, as would be expected, the stenosis of the right ventricle having an effect very like that of tricuspid stenosis. Similarly, the lung fields remain clear radiologically and at necropsy the lungs are surprisingly dry in spite of

gross oedema elsewhere. The circulation rate is not greatly slowed: in 2 of the authors' patients the arm-to-tongue time was only 28 seconds, whereas in ordinary congestive failure it is commonly well over 40 seconds. As slowing chiefly occurs in the pulmonary circulation, the results were taken to indicate relative freedom of the lungs from circulatory embarrassment. Although in 3 cases the electrocardiogram showed the expected left axis deviation, this was absent in one. In the other case right axis deviation was present. It has been suggested that the electrical axis may be affected by the bulging of the ventricular septum to the right, but the authors contend, from study of unipolar leads, that in such cases the heart is vertical, so the presence of left ventricular hypertrophy cannot cause left axis deviation. They conclude, therefore, that there are no cardiographic changes peculiar to Bernheim's syndrome. They consider that as the raised venous pressure is beneficial, anything which reduces it, such as venesection, or administration of digitalis or "aminophylline" might do harm. At necropsy the diagnosis is confirmed by demonstrating the absence of pulmonary congestion; in order to see the encroachment of the septum into the cavity of the right ventricle it is essential that the heart be cut transversely across at right angles to its long axis, midway between apex and base. Other conditions in which, in spite of conspicuous jugular vein engorgement, freedom from pulmonary congestion persists so that dyspnoea is slight, orthopnoea absent, and the lung fields remain clear, are constrictive pericarditis and tricuspid stenosis.

S. Oram

2844. **Mitral Stenosis in Later Life**

H. Cookson. *British Heart Journal* [*Brit. Heart J.*] **11**, 155–164, April, 1949. 13 figs., 12 refs.

It is pointed out that rheumatic heart disease with mitral stenosis is considered on clinical grounds to be uncommon after the age of 50, amounting to at most 6 to 10% of cases, although it is known that if the lesion is accompanied by hypertension life may be prolonged. Yet necropsy studies put the incidence of such cases at 9 to 33% and this suggests that the diagnosis is often missed in life.

The author's series consists of 37 patients with mitral stenosis and one with mitral incompetence, the ages being from 51 to 77 years. There were only 9 men and the predominance of women increased in each successive decade so that all patients over 70 were women. When first seen, 32 of the 38 patients had auricular fibrillation and one had paroxysmal fibrillation. Later, fibrillation occurred in another of the remaining 4 patients and 2 had paroxymal tachycardia. Diagnosis was made on the presence of a rough, low-pitched diastolic murmur heard best at the apex or occasionally at a short distance from it. It began very soon after the 2nd sound and was decrescendo, dying away as a rule before the 1st sound. If it did continue until the 1st sound it could give the impression of a crescendo presystolic murmur, even in the presence of auricular fibrillation. When aortic incompetence was present, as it was in 10 patients, mitral stenosis was not diagnosed on the finding of an apical murmur unless radiological changes characteristic of mitral stenosis were present. Apart from 2 cases with only a systolic murmur, but proven at necropsy, a mitral diastolic murmur had been heard in all, although in some prolonged auscultation was necessary, the murmur being quite inaudible except in prolonged diastole.

The author points out that it was not easy to determine the frequency of hypertension in these cases, as auricular fibrillation was almost invariable and aortic incompetence common. A minimum diastolic pressure of 100 mm. or more was found in 19 and a systolic pressure of 190 mm. or more in 12. Only one patient had a radiologically normal heart. Unlike the picture seen in young subjects, the aortic knob was always visible and even prominent. In 2 cases the oesophagus was displaced considerably to the left and backwards, and could be seen only by screening in the second oblique or face position.

The onset of auricular fibrillation appeared to mark a turning point in the life history of the patient, who had suffered little or no handicap before its onset. Systemic congestion then appeared. The absence or mildness of symptoms until late in life was not due to the slightness of the valvular stenosis, for 2 patients were found at necropsy to have extreme narrowing of the mitral valve, although neither had ever had congestive failure.

The author concludes that there is too much reluctance to diagnose rheumatic heart disease in the elderly.

S. Oram

2845. **Morbus Coeruleus. A Study of 50 Cases after the Blalock–Taussig Operation**

C. Baker, R. C. Brock, M. Campbell, and S. Suzman. *British Heart Journal* [*Brit. Heart J.*] **11**, 170–198, April, 1949. 14 figs., 17 refs.

In 1948 Campbell published (*Guy's Hosp. Rep.*, **97**, 1) the largest series of cases of morbus coeruleus operated upon in Britain at that time, namely, 18.

The present article by the Guy's Hospital team is an extension of this work. [Its illustrations and tables should be consulted in the original.] The number of cases has now reached 50. All underwent a systemic-pulmonary anastomosis, and all except 3 were thought to suffer from Fallot's tetralogy or some closely related form of congenital heart disease. In the other 3 the clinical picture was similar, but with left ventricular preponderance in the electrocardiogram, which usually indicates tricuspid atresia or stenosis with a non-functioning right ventricle. The patients have been followed up for 6 to 15 months. The youngest patient operated upon was 2½ years old and the oldest 27. It was felt that 5 is the earliest age at which operation should be carried out, although actually there was no evidence that operation was more dangerous or less successful at 3 years old. It was found dangerous to operate on patients over 20.

The degree of disability present before operation varied considerably; in one case even undressing provoked daily attacks of loss of control of limbs and semi-consciousness, while another patient could walk about 2 miles (3·2 km.) slowly. All had been cyanosed from early infancy and all had finger clubbing. It was found

that, if the disability were severe enough, relatively slight cyanosis was not as a rule a contraindication to operation. In all cases except one cyanosis was noticed before the age of 18 months, and was present at birth or soon after in 30. The average haemoglobin percentage was 137, the erythrocyte count 7·8 million per c.mm., haematocrit value 74, but apparently as the haemoglobin value rises above 130% the erythrocyte count and haematocrit value do not usually rise any farther, with the result that the colour index rises towards unity. In only 41 of the 50 was there a history of squatting. The mental development in all but 2 of these children was normal or above average, but although they were only slightly under the average height most of them were underweight so that their thinness was very obvious.

The heart was generally of normal size; anything more than very slight enlargement should raise a suspicion that the lesion is not Fallot's tetralogy, or is complicated by some other defect. There was generally a systolic murmur in the 2nd, 3rd, and 4th spaces on the left, but in 4 cases no systolic murmur was heard. No patient had a diastolic murmur. In some a thrill was present but was never of great intensity. The pulmonary 2nd sound was generally normal, and if it were much increased or drum-like it suggested that the lesion was not Fallot's tetralogy. Radiologically, less than one-half of the hearts were sabot-shaped, and three important negative points were the absence of pulsation in the lung roots, of more than the most trivial cardiac enlargement, and of undue prominence of the pulmonary artery. The aortic arch was left-sided in 36 cases. Angiocardiography was of value in delineating the branches of the aorta and the size and position of the pulmonary arteries. A film taken at 2 seconds generally demonstrated the shunt best. The two most striking features of the cardiogram were the large pointed P waves, especially in lead II, and the right ventricular preponderance.

The hazard was greatest in the theatre, death occurring either there or within a few hours of the patient's return to the ward. The postero-lateral approach was preferred to the usual antero-lateral and, although Blalock originally recommended using the side opposite to the aortic arch in all but adults and patients in their later teens, the left-sided approach was preferred in all cases unless angiocardiography suggested that the right pulmonary artery was small or absent, indicating that it would be dangerous to occlude the left branch while the anastomosis was made. It was considered inadvisable to employ the carotid or innominate artery. Penicillin therapy was started 24 hours before operation, and pre-operative instruction in breathing exercises was a routine. The patient was nursed in an oxygen tent on return to the ward and breathing exercises and postural coughing began as soon as the patient was conscious. Morphine should be used with great care. Usually a continuous murmur, like that heard over a patent ductus arteriosus, appeared. The commonest post-operative complication was pleural effusion, but luckily this was generally harmless. It developed in 32 of 43 cases after operation. The gravest complication was cerebral thrombosis which occurred in 3 of the 43 cases. The average time in bed was 7 days. Of the 50 patients, 7 died. In 3 patients no anastomosis could be performed. Of the remaining 40 cases no improvement occurred in 3. In 33 of the 50 cases the result is described as " almost perfect ". None of the patients seen a year after operation had failed to maintain or increase the improvement made after a few months. *S. Oram*

CORONARY OCCLUSION

2846. **Microscopic Changes in the Cardiac Ganglion Cells in Human Coronary Sclerosis.** (Mikroskopische Beobachtungen an den Herzganglien des Menschen bei Coronarsklerose)
H. HERMANN. *Virchows Archiv für Pathologische Anatomie* [*Virchows Arch.*] **316**, 341–372, 1949. 13 figs., bibliography.

The morphology of the cardiac ganglion cells from 25 persons suffering from coronary sclerosis was examined by Bielschowsky's method. Five hearts from young persons served as controls. Between 41 and 83% of the ganglion cells were either degenerating or degenerated, depending on the degree of vascular disease. The changes are described in great detail, but those most frequently seen were swelling of the cell, pyknosis, abnormal shape or fragmentation of the nucleus, defects or loss of the nuclear membrane, vacuolization of the cytoplasm, inclusion of newly-formed homogeneous substances and, less frequently, newly-formed hyperplasia, swelling, or fragmentation of intracellular and extracellular argentophil fibrils. But the author emphasizes that these changes are in no way pathognomonic of coronary sclerosis, as they have also been observed in a variety of other conditions, although in the latter the progressive changes predominate, while in the former the degenerative processes are most frequently observed.
R. Salm

2847. **Prodromal Appearances in Myocardial Infarction.** (О продромальных явлениях при инфаркте миокарда)
Y. G. ETINGER. Клиническая Медицина [*Klin. Med., Mosk.*] **27**, No. 3, 24–32, March, 1949. 4 figs., 10 refs.

In recent years it has become established that coronary occlusion is often due to haemorrhage into the intima of the coronary arteries from rupture of capillaries. The majority of observers believe that normal coronary arteries do not contain capillaries, but that these develop as a reaction to the arteriosclerotic process; they are not all derived from the vessels of the adventitia, but may arise from the lumen of the artery itself. Rupture of the capillaries may lead to obliteration of the arterial lumen, or to thrombosis due to necrosis or erosion of the intima. According to Paterson, two factors may lead to haemorrhage—softening of the atheromatous plaques, and increase of intracapillary pressure as a result of physical or emotional strain. Thus a vicious circle is set up; softening of plaques leads to haemorrhage, while this in turn leads to breaking down of the plaques.

Thrombosis is a slow affair, whereas occlusion due to sudden intravascular haemorrhage is rapid. Usually some coronary insufficiency precedes the actual

thrombosis and its presence is indicated by anginal pain on exertion or even at rest. At this stage, symptoms are relieved by trinitrin; the electrocardiogram shows evidence of coronary insufficiency. Later, when thrombosis takes place, other changes are seen in the electrocardiogram, notably low voltage of waves and a polyphasic character of QRS in lead I, the disappearance of the R wave in the chest leads, and elevation of ST.

The author emphasizes the importance of recognizing the earlier changes and instituting a regimen of complete rest, which may prevent the onset of the more serious later changes in some cases and in others enable the patient to survive the crisis. He quotes 6 of his own cases in support of his thesis, and illustrates them with series of electrocardiographic tracings taken in the pre-thrombotic and post-thrombotic stages.

[This article confirms the generally accepted views on the evolution of coronary thrombosis, but adds little new to our knowledge of the subject.]

L. Firman-Edwards

2848. **Clinical Diagnosis of Painless Myocardial Infarction.** (О клиническом диагнозе безболевых инфарктов миокарда)
N. I. Speranskii. Клиническая Медицина [*Klin. Med. Mosk.*] **27**, No. 3, 32–35, March, 1949. 8 refs.

Infarction of the myocardium may in some instances give rise to no pain, and diagnosis may consequently be very difficult. The author gives five examples of such cases, diagnosed during life and confirmed by necropsy. The presenting symptom was either acute cardiac asthma, or dyspnoea with oedema, sudden weakness, and vertigo. The former is especially common in infarcts of the left ventricle. All these cases occurred in persons apparently healthy before the onset of symptoms, yet in some cases numerous infarcts were found post mortem. Though clinical signs may be misleading, the electrocardiogram will reveal the nature of the condition. The important step is a careful analysis of the history of the case; if the possibility of painless infarction is borne in mind, the sudden onset of symptoms of cardiac distress in the absence of extracardiac cause will lead to the necessary investigations being made.

L. Firman-Edwards

2849. **Apoplectiform Syndrome in Myocardial Infarction.** (Апоплектиформный синдром при инфарктах миокарда)
N. K. Bogolepov. Клиническая Медицина [*Klin. Med., Mosk.*] **27**, No. 3, 36–40, March, 1949. 4 figs.

The author describes 3 cases in which infarction of the heart produced symptoms so similar to apoplexy that the patients were admitted to the neurological ward. In all these cases, which were rapidly fatal, necropsy revealed a recent infarct of the myocardium and the only findings in the brain were congestion and stasis in the vessels of the brain stem with small haemorrhages and some perivascular oedema. He gives 4 criteria which should lead to suspicion of the coronary origin of such crises: (1) Vertigo is frequently the first symptom. (2) General weakness may be the initial symptom, leading in a short while to paralysis of all four limbs. (3) Pain is referred to the retrosternal area, radiating to the left arm. (4) A severe fall in blood pressure and a scarcely perceptible pulse may be noted. He claims that an infarct of the anterior wall of the ventricle is liable to cause these symptoms, as there is a close connexion between the plexus supplying this part of the ventricle, the aortocarotid plexus, and the vasomotor centres of the brain stem. Infarcts of the posterior wall of the left ventricle, on the other hand, may give rise to the abdominal syndrome.

L. Firman-Edwards

2850. **The Electrocardiogram in Myocardial Infarction: its Value as a Diagnostic Aid in 130 Autopsied Cases**
R. B. Failey. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **217**, 283–293, March, 1949. 14 refs.

The author reviewed 100 cases of myocardial infarction proved at necropsy and 30 cases in which a clinical diagnosis of myocardial infarction was seriously considered and not confirmed at necropsy, with the object of determining the value of electrocardiography in the diagnosis of this disease. The majority of the electrocardiograms were taken with the three standard leads and lead CF4 or V4. In certain cases multiple chest leads and the three unipolar extremity leads were also used. Only 55 of the proved cases had been adequately investigated electrocardiographically; the infarction was correctly diagnosed in 29 of these. Of 22 cases of recent anterior infarction the electrocardiographic diagnosis was correct only in 8 when 4 leads were taken, but was correct in all 5 cases in which multiple precordial leads were taken. With recent posterior infarction the diagnosis was made electrocardiographically in 5 of 8 cases when only 4 leads were taken, but in 4 out of 5 cases when 12 leads were used. Sixteen of the 30 cases incorrectly diagnosed on clinical grounds as cases of infarction were studied electrocardiographically; in 5 cases the electrocardiogram supported the incorrect diagnosis, in one the electrocardiogram typical of acute pericarditis was wrongly interpreted as indicating infarction. From this analysis it is concluded that the use of 6 precordial leads as a routine is of great value in the accurate diagnosis of myocardial infarction, while unipolar extremity leads appear to be of comparatively little value.

C. Bruce Perry

HYPERTENSION

2851. **The Treatment of Hypertension with Hexanitro-meso-inositol.** (Le traitement de l'hypertension par l'hexa-nitro-méso-inositol)
P. Balatre, J. F. Merlen, and L. Grandjean. *Thérapie* [*Thérapie*] **3**, 209–211, 1948. 1 fig., 3 refs.

The authors have treated 42 cases of hypertension with hexanitro-meso-inositol (20 to 40 mg. daily by mouth in eight 5 mg. doses, in short courses lasting for 12 to 15 days with intervals of 8 to 10 days). This drug is virtually non-toxic (the LD 50 for rats is 1 g. per kg. body weight and the therapeutic dose is 1 mg. per kg.) and no control

of the level in the blood is needed. The symptoms noted while the drug was being taken were indigestion, nausea, and asthenia. The results obtained are similar to those obtained with other hypotensive agents, successes and disappointments occurring as with drugs such as potassium thiocyanate and aminophylline, and with sedatives.

Although the number of cases treated is small it is clear that results are comparable with those obtained with other drugs, but the advantages of non-toxicity lead the authors to suggest further trials inhypertens ion.

John Anderson

2852. **Immediate and Prolonged Action of Injections of Vitamin A in the Treatment of Persistent Arterial Hypertension.** (Action immédiate et prolongée des injections de vitamin A dans le traitement des hypertensions artérielles permanentes)

R. LECOQ and L. BRUEL. *Thérapie* [*Thérapie*] **3**, 212–218, 1948. 14 refs.

The authors have previously published work on the hypotensive effects of intramuscularly administered vitamin A. They point out that synthetic vitamin A is inactive and that some oily preparations are also inactive because they are not absorbed after injection or are incorrectly injected; furthermore, skin antiseptics may destroy vitamin A. Dhotel laid stress on the use of the vitamin by intravenous injection, a method fraught with danger. The authors have produced a watery vehicle for vitamin A which is quite safe. Anaphylaxis may occur but can be aborted by the usual measures. The dose of the preparation is 2 ml. containing 30,000 i.u. vitamin A and administered intravenously at 7-day intervals.

Eleven hypertensive patients received 3 to 5 intravenous injections, with a resulting hypotensive effect [the follow-up was insufficient to bear out the claim for a prolonged effect]. A further 6 cases are reported, to illustrate the prolonged effect of vitamin A. [No report is given of the method of manufacture of the watery solution for which these results are claimed, and although the intravenous vitamin A appears to have reduced the blood pressure the number of cases is very small. The future reports by this group should be watched for, and if the method of preparation is disclosed intravenous vitamin A should be given a trial by other workers.]

John Anderson

2853. **Values of Hypertensin and Hypertensinogen in the Blood of Patients with Renal Hypertension.** (Les valeurs de l'hypertensine et de l'hypertensinogène dans le sang des malades avec hypertension rénale)

V. ZELENKA and E. EISEL. *Revue Médicale de Liège* [*Rev. méd. Liège*] **4**, 231–234, April 15, 1949. 19 refs.

From the Institute of Physiopathology and Medical Clinic, Prague, the authors report on the concentration of hypertensin and hypertensinogen in the blood of two groups of patients—those with primary and those with secondary hypertension. In the first group were 10 patients with benign and malignant nephrosclerosis and with essential hypertension; in the second group, 4 patients suffering from acute, subacute, and chronic nephritis.

In 5 patients with malignant nephrosclerosis there was a constant pronounced elevation of systolic and diastolic blood pressure associated with greatly increased arterial tension and, in all but one, a raised non-protein nitrogen (N.P.N.) level. All had characteristic changes in the retinal blood vessels, with signs of cardiac impairment and apical gallop rhythm which disappeared on treatment. A definitely raised blood hypertensin concentration and a lowered free hypertensinogen level occurred in all. Two patients with benign nephrosclerosis had slight hyperpiesia and sclerosis of the retinal vessels. The level of hypertensin was lower, and of hypertensinogen higher, than in the subgroup with malignant nephrosclerosis.

The 3 patients who were suffering from essential hypertension were at different clinical stages of the disease: one whose blood pressure returned to normal after rest in bed had an almost normal hypertensin concentration; one with moderate permanent diastolic hypertension but normal optic disks had moderately raised hypertensin and hypertensinogen levels; while the third patient, who had much increased diastolic pressure, retinal changes, and cardiac failure, also had raised hypertensin and hypertensinogen levels. One patient, with residual hypertension after recovery from acute nephritis, had a small amount of hypertensin in the urine and marked reduction in plasma hypertensinogen level, suggesting an adequate concentration of hypertensinase in his tissues. Two patients with subacute nephritis had almost identical hypertensin and N.P.N. values and water dilution and concentration test figures, but in one the blood pressure was normal and in the other raised, the hypertensinogen level in the former being reduced.

One patient with chronic nephritis who was admitted to hospital in uraemic coma with brisk haematuria, a blood pressure of 205/125 mm. Hg, and a N.P.N. level of 167 mg. per 100 ml., was treated with hypertensinase. Blood pressure and N.P.N. level fell to normal and the hypertensin concentration was decreased, but that of hypertensinogen was almost normal. In this case it is concluded that the hypertensin level, and with it the arterial blood pressure, were reduced by parenteral administration of hypertensinase in the form of extract of renal pulp; when this treatment was stopped the blood pressure rose to 280/140 mm. The blood of one normal control contained no hypertensin, and hypertensinogen concentration was diminished in patients with liver disease.

The interrelationship of hypertensin, hypertensinogen, and hypertensinase are discussed, and the techniques and units of measurement employed in their estimation are [somewhat inadequately] outlined.

Walter H. H. Merivale

See also Sections Endocrine Disorders, Abstract 2933 (*a*) and (*b*); Venereal Diseases, Abstract 2966; Neurology, Abstract 2996.

Disorders of the Blood

2854. **The Myelogram Before and After "Pentnucleotide."** (Mielogramma prima e dopo pentanucleotide)
V. GALLO and A. GRIGNANI. *Haematologica* [*Haematologica*] **33**, 71–88, 1949. 18 refs.

After the administration of "pentnucleotide" in 5 cases the number of leucocytes increased in the peripheral blood. In the marrow in 7 cases the number of proerythroblasts and basophilic normoblasts decreased, that of the polychromatic normoblasts varied, and that of the orthochromatic normoblasts definitely increased. The count of myeloblasts, promyelocytes, and myelocytes decreased, but that of metamyelocytes increased markedly. Calculation of the various ratios between cells of the erythroid and myeloid series confirmed these findings. *E. Neumark*

2855. **A Basis for Discussion of the Nomenclature of Blood Cells.** (Rapport pour servir à la discussion sur la nomenclature des cellules du sang)
P. CHEVALLIER. *Sang* [*Sang*] **20**, 330–348, 1949.

This is a contribution to the terminology of haematology, with a criticism of that suggested in America. [The paper should be read in detail by all those who may take part in formulating a definitive nomenclature.] *A. Piney*

See also Sections Physiology and Biochemistry, Abstract 2671; Infectious Diseases, Abstract 3060.

2856. **Circulating Anticoagulants: A Technique for their Detection and Clinical Studies**
C. L. CONLEY, R. C. HARTMANN, and W. I. MORSE. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **84**, 255–268, March, 1949. 1 fig., 18 refs.

The presence of anticoagulants in serum can be determined by withdrawing blood into silicone-coated syringes fitted with silicone-coated needles. Blood so obtained is centrifuged in silicone-coated tubes at 6,000 revolutions per minute (r.p.m.) for 5 minutes to remove erythrocytes, and the separated plasma similarly centrifuged at 12,000 to 14,000 r.p.m. for 10 minutes to remove platelets; the platelet-free plasma is then tested for its capacity to delay clotting of normal blood. The latter is collected in silicone-coated vessels, but for clotting tests is put into scrupulously clean "pyrex" tubes. Plasma concentrations of 0·001 mg. or more of heparin per ml. give distinctly positive reactions, even if the amounts injected are insufficient to affect the clotting time of the whole blood.

Of 41 subjects examined, in only 8 was evidence of circulating anticoagulants found; of these latter, only one showed reversal with toluidine blue, and is presumably a heparin-like substance. [As is indicated in this paper, considerable caution is needed in using toluidine blue to reverse the heparin effect, as toluidine blue is itself a powerful anticoagulant, and if added in excess may increase, instead of reducing, the coagulation time.] Of the 6 haemophilic patients only one had a circulating anticoagulant. One positive example was found in a patient suffering from a *Clostridium welchii* septicaemia and thrombocytopenia. The remaining 5 patients included one with dicoumarol poisoning, 2 regarded on clinical grounds as having circulating anticoagulants, and 2 with severe liver disease.
C. L. Oakley

2857. **Does Eosinophilic Leukaemia Exist?** (La leucémie à éosinophiles existe-t-elle?)
A. PINEY. *Revue d'Hématologie* [*Rev. Hémat.*] **4**, 3–5, 1949. 13 figs., 10 refs.

The author quotes the case of a girl of 18 who presented the typical clinical picture of acute leukaemia with multiple haemorrhages. The disease ran a rapidly fatal course, but necropsy was not permitted. The peripheral blood contained 80,000 leucocytes per c.mm. of which 54% contained eosinophil granules, the proportion rising later to 71%. Some of these cells were classed as promyelocytes and myelocytes, but blast cells were not found. The marrow was packed with eosinophil myelocytes. The case is presented as another unequivocal example of "eosinophil leukaemia". *P. C. Reynell*

ANAEMIA

2858. **Preparation and Standardisation of Saccharated Iron Oxide for Intravenous Administration**
J. A. NISSIM and J. M. ROBSON. *Lancet* [*Lancet*] **1**, 686–689, April 23, 1949. 7 figs., 2 refs.

The authors describe a method for the preparation and biological standardization of saccharated iron oxide in a form suitable for intravenous administration. The ferric hydroxide obtained by the addition of ferric chloride to sodium carbonate yields better and more constant results than when prepared in other ways. In this reaction ferric carbonate is first produced, and this is subsequently hydrolysed to form ferric hydroxide. The ferric hydroxide giving the most soluble sucrate was produced by dissolving ferric hydroxide in excess of ferric chloride and re-precipitating it with sodium carbonate.

The authors found that the amount of alkali, sucrose, and carbonate could be varied as well as the *p*H of the precipitation point, and each of these factors was independently investigated. Toxicity tests designed to evaluate the effect of these variable factors were also carried out on female white mice. In animals given lethal doses of saccharated iron oxide macroscopic haemorrhagic lesions invariably appeared, being most evident in the lungs and having the appearance of infarcts. Intestinal haemorrhages were frequent and haemoptysis

was occasionally noted; lesions were also found in the liver, kidneys, and heart. In the few animals in which macroscopic lesions were not observed, histological evidence of haemorrhage was seen in the lungs and liver, and considerable deposits of iron were also found in these organs. The occurrence of such lesions suggests that with large doses the iron precipitates slowly in the blood plasma and gives rise to multiple capillary embolism.

Although saccharated iron oxide appears to be stable when in contact with sterile plasma *in vitro*, it appears to undergo precipitation *in vivo*. The authors suggest that the precipitation may be due to the gradual breakdown of the compound as the sugar part of the molecule is metabolized, and that its toxicity is directly proportional to its rate of metabolism and inversely proportional to the rate at which it can be removed from the blood by the reticulo-endothelial system.

A sample of saccharated iron oxide containing 16·6 g. of sucrose per gramme of iron was tested clinically. Several patients received repeated doses of as much as 300 mg. of iron by intravenous injection without toxic effect. Each of these injections was equivalent in iron content to 1½ pints (852 ml.) of blood. The authors conclude that preparations of saccharated iron oxide for clinical use will have to be standardized biologically to make sure that their toxicity is not too high, until a method of preparation which yields consistent samples is evolved. *R. Winston Evans*

2859. **Importance of Iron Absorption Studies in the Diagnosis and Differential Diagnosis of Anaemias due to Iron Deficiency, and Especially in the Recognition of Iron Lack without Anaemia.** (Die Bedeutung der Eisenresorptionsversuche für die Diagnose und Differentialdiagnose der Eisenmangelanämien, insbesondere für die Erkennung der Eisenmangelzustände ohne Anämie) B. JASIŃSKI. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **79**, 291–293, April 2, 1949. 5 figs., 8 refs.

The author investigated the absorption of iron by estimating the serum iron concentration before, and at 1, 3, 7, 10, and 14 hours after, the oral administration to the fasting human subject of the equivalent of 176–198 mg. of divalent iron in the form of 8 to 9 tablets of "FSO 142" (ferrogluconate). He was impressed by the quantitative difference in the absorption of iron in cases of so-called "essential" iron deficiency anaemia and in those of chronic post-haemorrhagic iron deficiency anaemia.

Essential iron deficiency anaemia seems to arise from poor utilization of ingested iron, an important contributory factor being menstrual loss, this form of anaemia being unknown in males and rare before puberty. The case is described of a girl aged 16, menstruation not begun, whose father had severe pernicious anaemia, and who for 5 years had complained of increasing pallor, fatigue, and occasional abdominal pains. She had flat, brittle nails, rhagades, and a smooth tongue, with some underdevelopment, but good general nutrition. Her blood haemoglobin level was 32%, and her erythrocytes 3,100,000 per c.mm., and markedly hypochromic; achlorhydria was present and the faeces contained no occult blood. Her serum iron level before, and 1, 3, and 7 hours after ingestion of iron was 32, 108, 28, and 8 μg. per 100 ml. respectively—absorption relatively low, characteristic of essential iron deficiency anaemia. A second case which appeared clinically to be of the essential type occurred in a man aged 50, working in contact with lead and cyanide, with a history of 5 years of pallor, precordial oppression, and fatigue. His haemoglobin level was 52%, erythrocytes 4,000,000, markedly hypochromic; stomach acidity was normal and the faeces occasionally faintly positive to the benzidine test. However, his serum iron level before, and 1, 3, and 7 hours after ingestion of iron was 28, 192, 352, and 184 μg. per 100 ml. respectively—normal absorption characteristic of a post-haemorrhagic iron deficiency anaemia. Further investigation revealed the site of slight bleeding to be in the stomach, which had passed retrocardially through a large diaphragmatic hernia.

Iron absorption tests are of particular value in the recognition of states of iron deficiency without anaemia, a condition detected by Waldenström, J. (*Acta med. scand., Suppl.*, 1934, **90**, 380 and *Schweiz. med. Wschr.*, 1944, **74**, 978). The diagnosis is not difficult if dysphagia, cheilitis, and koilonychia are present, but in their absence the only presenting symptoms may be fatigue, headache, dyspnoea, and palpitation. The cases are reported of 2 women under treatment for confirmed gastric ulcer who had no evidence of blood loss or anaemia, but complained of excessive tiredness and weakness. Their serum iron level was found to be very low and their response to the absorption test poor. The serum iron level was restored to normal after some weeks of oral iron therapy, when the patients became symptom-free and fit, the gastric ulcer having healed in each case. The author regards these as cases of essential iron deficiency in which exhaustion of depot iron reserves had not yet affected haemoglobin formation. Such cases may persist for years before anaemia develops, and might be more commonly recognized if iron absorption tests were more frequently made. [The method used to estimate the serum iron concentration is not given.] *Dushanka Wolstenholme*

See also Section Digestive Disorders, Abstract 2909

2860. **Response of Lingual Manifestations of Pernicious Anemia to Pteroylglutamic Acid and Vitamin B_{12}** J. F. SCHIEVE and R. W. RUNDLES. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 439–447, April, 1949. 3 figs., 31 refs.

The effect of pteroylglutamic acid therapy in pernicious anaemia was found to be variable in respect of associated pathological changes in the tongue. In some patients the response was good, in others poor. Two patients are described who gave satisfactory clinical and haematological response to folic acid in daily doses of 30 to 50 mg., but developed severe glossitis in the third month of treatment. Vitamin B_{12} was then given intramuscularly in doses of 0·05 and 0·025 mg. respectively, and was in each case followed by a prompt lingual

response. In 4 other cases of pernicious anaemia existing lingual manifestations did not respond adequately to folic acid therapy but did so to subsequent treatment with liver extract. In 5 patients with tongue changes who were treated initially with parenteral vitamin B_{12} in doses varying from 0·001 mg. daily to a single dose of 0·01 mg. regeneration of the lingual papillae occurred in 5 to 7 days. On the other hand, in 2 further cases folic acid therapy resulted in a rapid restoration of normal lingual mucosa, although in one of these cases the haematological remission was incomplete. In several of the patients folic acid appeared to exert a favourable effect on neurological manifestations.

The significance of these observations is discussed, and it is concluded that pteroylglutamic acid has an irregular effect on all manifestations of pernicious anaemia rather than failing consistently in any one of them. The cause of this variability remains to be determined.

L. J. Davis

2861. **Treatment of Pernicious Anemia with Crystalline Vitamin B_{12}**

R. West and E. H. Reisner. *American Journal of Medicine* [*Amer. J. Med.*] **6**, 643–650, May, 1949. 3 figs., 16 refs.

In all of 11 cases of Addisonian pernicious anaemia treated with crystalline vitamin B_{12} there were satisfactory haematological response and restoration of normal blood level. The substance was injected intramuscularly, the weekly dosage being 25 μg. or less. The minimium effective dose was found to be 1 μg. daily. Five of the patients with spinal-cord lesions showed varying degrees of improvement; none of them deteriorated. The relation between thymine, folic acid, cobalt, and vitamin B_{12} is discussed, and the view is advanced that vitamin B_{12} is probably the erythrocyte maturation factor of liver.

[Recent reports of cases of megaloblastic anaemia failing to respond to vitamin B_{12} but responding to folic acid would suggest that vitamin B_{12} is not the sole erythropoietic factor.] *L. J. Davis*

2862. **The Pathological Physiology of the Bone Marrow in Pernicious Anaemia. The Problem of the Megaloblast.** (Contribution à l'étude de la physiopathologie de la moelle osseuse dans la maladie de Biermer. Le problème du mégaloblaste)

L. Fruhling, S. Roger, and H. Spehler. *Sang* [*Sang*] **20**, 164–195, 1949. 11 figs., bibliography.

The authors studied 40 cases of pernicious anaemia. In 12 of them they performed repeated sternal punctures, recording the numbers of cells in the marrow juice as well as differential counts of cells in smears. The range of cell count for normal marrow had previously been found to be 25,000 to 55,000 per c.mm., with a mean of 37,000 (*Sang*, 1948, **19**, 305). In most cases of untreated pernicious anaemia the initial cell count was increased (range 33,000 to 338,000; mostly 100,000 to 300,000 per c.mm.). When liver extract or folic acid was administered, a fall in the cell count to half its initial value or less occurred between the 15th and the 24th hour, and was followed by a secondary increase after about 3 days to about 80,000 per c.mm. and thereafter a slow fall to normal levels. In smears taken between the 15th and the 24th hour after liver injection massive degeneration and lysis of the megaloblasts were seen, the nuclei becoming homogeneous and hydropic, and smear cells being more common. Simultaneously, the clotting time of the marrow juice was greatly reduced. A few hours later normoblastic erythropoiesis was well established, and normoblastic hyperplasia was maximal by the 3rd day.

These results demonstrated that the effect of liver therapy is not to convert megaloblasts into normoblasts, but to permit the new formation of normoblasts from their precursors, while pre-existing megaloblasts degenerate *in situ*. This explains the slight evanescent fall in the erythrocyte count observed on the 1st and 2nd days of treatment, the increase in uric acid and phosphate excretion on the 2nd and 3rd days, and the delayed reticulocyte response.

The authors arrive at the following conclusions: (1) megaloblasts cannot be transformed into normoblasts; (2) megaloblasts are cells suffering from simultaneous disorders of development and maturation; and (3) " intermediate " megaloblasts are megaloblasts suffering from a minor degree of disordered development; they are not transitional stages between megaloblast and normoblast.

[This important paper should be read in full by all haematologists. It supports the Ehrlich–Ferrata theory of erythropoiesis, and is the most convincing exposition of this subject which the abstracter has yet read.]

G. Discombe

2863. **The Marchiafava Micheli Syndrome (Paroxysmal Nocturnal Haemoglobinuria)**

J. Marks. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **18**, 105–121, April, 1949. 3 figs., bibliography.

The author reviews the literature on the Marchiafava Micheli syndrome and describes 3 new cases, bringing the total number so far reported to 76. Various aspects of the condition are described in detail. The disease is neither hereditary nor racial, it affects the sexes equally, and may begin at any age, although its onset is most commonly between 20 and 40 years. The disease does not always present primarily with haemoglobinuria. The earliest symptoms in the 73 cases previously described in the literature were: haemoglobinuria (33), anaemia or dependent symptoms (36), jaundice (27), lumbar pain (7), abdominal pain (5), and splenomegaly (2). The most common complication is thrombosis. The chronic anaemia with granulocytopenia favours the development of intercurrent infection which is often terminal.

The cause of the condition is unknown. The primary abnormality lies in the erythrocytes, which undergo lysis by a thermolabile fraction of normal serum. The haemolysin is sensitive to changes in *p*H, but it may be that changes in the concentration of certain ions in the plasma rather than changes in *p*H during sleep are responsible for the nocturnal character of the haemoglobinuria. No cure for the disease is known and the prognosis is poor. The average expectation of life is

7 to 10 years from the onset of symptoms. Splenectomy appears to be contraindicated. There is an immediate mortality of about 40% from this operation, and no patient who has survived it has been demonstrably improved. The acid serum haemolysis test of Ham and the heat test of Hegglin and Maier are described in detail. *A. Brown*

2864. **Survival of Transfused Erythrocytes from a Donor with Nocturnal Haemoglobinuria**
J. V. DACIE and P. L. MOLLISON. *Lancet* [*Lancet*] **1**, 390–392, March 5, 1949. 3 figs., 10 refs.

The authors give a detailed account of the survival rate of erythrocytes taken from a patient suffering from nocturnal haemoglobinuria (Marchiafava–Micheli disease) and transfused into an adult and an infant. The donor's blood group was O, Rh-positive, and in the first instance 420 ml. of his blood mixed with 120 ml. of acid sodium citrate and glucose diluent was transfused into a group B adult patient and the survival rate of the transfused erythrocytes studied by a modified differential agglutination technique. In the second instance 170 ml. of the donor's blood was mixed with 50 ml. of the anticoagulant solution; next morning 35 ml. of a slightly concentrated suspension of the erythrocytes, together with 25 ml. of a more concentrated erythrocyte suspension from a normal group A, Rh-negative donor, was transfused into an Rh-positive premature infant of group A.

The survival rate of the donor's erythrocytes in the adult recipient showed that they were eliminated more rapidly than normal, 50% disappearing from the recipient's circulation in 5 days. Elimination of the remaining erythrocytes was slower, 20% surviving for over 20 days. In the infant elimination was less rapid, 50% disappearing in about 12 days, whereas the rate of elimination of the erythrocytes from the normal donor was approximately 1% a day.

In tests carried out *in vitro* the degree of haemolysis of erythrocytes from the patient with nocturnal haemoglobinuria was notably less in the baby's serum than in other sera tested. *R. Winston Evans*

2865. **Survival after Transfusion of Rh-Positive Erythrocytes Previously Incubated with Rh Antibody**
P. L. MOLLISON and J. C. S. PATERSON. *Journal of Clinical Pathology* [*J. clin. Path.*] **2**, 109–113, May, 1949. 2 figs., 7 refs.

Erythrocytes from a case of acquired haemolytic anaemia were found, in previous experiments, to survive normally in a normal recipient, in spite of the fact that the donor's erythrocytes were coated with an incomplete antibody. In order to discover what happens to the antibody coating of sensitized erythrocytes when the latter are transfused to normal people the present investigation was made.

Blood sensitized artificially with "incomplete" or blocking Rh antibodies was transfused to 5 Rh-positive subjects, and the survival time of the transfused blood followed by the Dacie and Mollison modification of Ashby's technique. There was evidence that some Rh antibody became detached from the erythrocytes and transferred to those of the recipients. There were, however, no signs of increased rate of destruction of recipients' erythrocytes due to this "sensitization".

In the test-tube, the transference of antibody from sensitized cells to normal Rh-positive cells could be demonstrated when the two were mixed. It was found impossible to remove the antibody from sensitized cells by incubation [presumably at 37° C.] with normal plasma, as estimated by the strength of the Coombs reaction and also by antibody tests on the plasma.

The authors find that transfused erythrocytes which have been previously sensitized retain their antibody coating for long periods after transfusion and that the bulk of the transfused cells survive normally. The findings are compared with those of Owren and the discrepancies are discussed. The authors suggest that the sensitization of cells only determines the haemolysis of erythrocytes in the body when a minimal quantity of coating antibody is exceeded; alternatively, that the antibody detected by the Coombs test does not cause haemolysis by itself or even with the assistance of any normal component of plasma. They conclude that a positive direct Coombs test cannot by itself be taken as evidence that erythrocytes are being destroyed at an abnormal rate. *John Murray*

HAEMATOPOIETIC SYSTEM

2866. **Antihistaminic Drugs and Agranulocytosis.** (Antihistamine praeparaten en agranulocytose)
J. A. VAN LOON and J. A. C. KANTERS. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **93**, 1070–1074, April 2, 1949. 3 refs.

In a 38-year-old pregnant woman agranulocytosis was provoked by "antistin" and "antallergan" administered for an itching skin affection (4 drops of antistin thrice daily and 50 tablets antallergan over 8 days). The agranulocytosis was treated by blood transfusion and administration of "pentnucleotide" and penicillin, and the patient recovered. A remarkable leukaemic reaction developed during therapy; a maximum of 56,000 leucocytes per c.mm., with myeloblasts, promyelocytes, and myelocytes, was observed on the ninth day of treatment. *A. W. Kamerling* (*Excerpta Medica*)

2867. **The Role of Infection in Granulopenia**
K. ROBERTSON. *British Medical Journal* [*Brit. med. J.*] **1**, 799–801, May 7, 1949. 11 refs.

The cases are reported of 4 men in whom oral sepsis and granulopenia developed during arsenic (neoarsphenamine) and bismuth treatment for syphilis. Under treatment with penicillin alone both the oral sepsis and the granulopenia cleared up; the only delay occurred in one patient infected with penicillin-resistant staphylococci, but he responded when the dosage of penicillin was doubled. Two of the patients were again given 0·3 g. neoarsphenamine after recovery, but no granulopenia occurred; one man had a transient urticaria. The author therefore supports the view of Dameshek and others that control

of infection is of primary importance in the treatment of granulopenia, and that, failing this, treatment with so-called marrow stimulators, such as "pentnucleotide," will be of little value. Large doses of penicillin, up to 1,000,000 units daily, should be used.

M. C. G. Israëls

2868. **Haematopoiesis and Blood Destruction in Some Aspects of Respiratory Insufficiency.** (Кроветворение и кроворазрушение при некоторых видах дыхательной недостаточности)

K. N. SEMENOVA. Клиническая Медицина [*Klin. Med., Mosk.*] **27**, No. 5, 40–51, May, 1949. 15 refs.

The apparatus of external respiration, that of blood circulation, and the blood itself form a single system ensuring the internal respiration. Oxygen deficiency is one of the most potent stimulants of the haematopoietic system. It causes not only more rapid maturation and production of erythrocytes, but also an accelerated passage of young erythrocytes from the marrow into the peripheral circulation. This is shown by the increase in haemoglobin concentration and polycythaemia which occur in dwellers at high altitudes, and in sufferers from chronic pulmonary disease and congenital heart disease.

Numerous workers (including Sirotinin) observed a fall in the erythrocyte count in the first stage, followed by a rise, during which the haemoglobin value lags behind. This has led Sirotinin and others to postulate an increased destruction of erythrocytes under conditions of oxygen lack. Fick, however, demonstrated a diminished destruction of erythrocytes and a prolongation of their life cycle in hypoxaemia. Heilmeyer and others found that the haemoglobin concentration, erythrocyte count, and cell volume of the blood increased by an average of 13% after 18 days at an altitude of 2,650 m. There was an increase in reticulocytes during the first 2 to 3 days. The quantity of urobilin in the stools fell under these conditions, while that in the urine rose slightly. On return to lower levels, all these changes were reversed.

In the present investigation the blood changes under certain conditions of respiratory insufficiency were studied in 44 patients—19 with chronic emphysema, 18 with pneumosclerosis, and 7 with post-asthmatic emphysema; 35 were men and 9 women. They were divided into three groups: those dyspnoeic on exertion, those dyspnoeic at rest, and those showing in addition signs of cardiac insufficiency. Erythropoiesis was measured by estimating reticulocytes, haemoglobin value and erythrocytes, cell volume, and the size and shape of erythrocytes. The serum bilirubin level, the stercobilin level in the stools, and the urinary urobilinogen concentration were also recorded. The average findings in 14 controls were taken as the normal values.

Under the hypoxaemic conditions of pulmonary insufficiency, the following changes were observed: (1) There was a rise in the colour index, in reticulocyte count, in mean corpuscular volume, and in the diameter and thickness of erythrocytes. There was no change in the fragility of erythrocytes. (2) The faecal stercobilin increased in proportion to the degree of respiratory insufficiency. (3) The urinary urobilinogen concentration remained within normal limits. (4) These changes all bore a relation to the degree of insufficiency, and became less marked after oxygen treatment, but never returned to normal levels. These findings can be explained by an increased erythropoiesis accompanied by increased blood destruction.

L. Firman-Edwards

2869. **Bone Marrow Studies in the Polycythemia of High Altitudes**

C. F. MERINO and C. REYNAFARJE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 637–647, May, 1949. 5 figs., 29 refs.

The sternal marrow of 16 healthy adult Indians, permanent residents in Cerro de Pasco, at an altitude of 4,390 metres (14,400 ft.), was studied. In all of them a polycythaemia was present in the peripheral blood; the number of leucocytes and platelets was within normal limits. Hyperplasia was found in 81·2% of the specimens examined and was due to an increase in the erythroid series of cells, mainly a normoblastic hyperplasia. There was no deviation from normal in the myeloid cells and megakaryocytes, and the myeloid–erythroid ratio was 1 to 1·4. The authors compare these results with those obtained in cases of polycythaemia vera, where, in general, there is hyperplasia of all cell elements, including megakaryocytes, and the myeloid–erythroid ratio remains approximately normal. Their findings afford further evidence that anoxia acts as a specific stimulus for an increased activity in the formation of the erythroid cells, leaving the myeloid cells unaffected, and that anoxia is not the underlying aetiological factor in polycythaemia vera.

A. W. H. Foxell

2870. **Acute Erythroblastopenia. Ten Cases of Aplastic Erythroblast Crisis with Giant Proerythroblasts in Allergic Subjects.** (Akute Erythroblastopenie. 10 Fälle aplastischer Erythroblastenkrisen mit Riesenproerythroblasten bei allergischtoxischen Zustandsbildern)

C. GASSER. *Helvetica Paediatrica Acta* [*Helv. paediat. Acta*] **4**, 107–143, May, 1949. 14 figs., 25 refs.

In the bone marrow of 10 children, between 1½ and 10½ years old, suffering from various illnesses, there was a sudden and almost complete disappearance of erythroblasts, while pathological giant cells resembling proerythroblasts appeared. During the erythroblastopenic period reticulocytes disappeared from the blood and marrow.

In 5 cases there were allergic phenomena, in 1 case chorea, in 2 cases haemolytic icterus, in 1 case a history of persistent granulocytopenia during infancy, and in 1 case congenital heart disease. The erythroblastopenia was always of only a few days' duration, and was followed by rapid return to normal. It is considered that an allergic constitution was the underlying cause, eosinophilia occurring in all cases, but various precipitating factors were present, for example, an insect bite in 1 case, treatment of worms with oil of chenopodium in 2 cases, and, perhaps, a virus infection in others. There is an

obvious similarity between this syndrome and the hypoplastic phases of spherocytosis described by Owren (*Blood*, 1948, **3**, 231). The discovery of this malady completes the triad of which only two members were known, namely, benign granulocytopenia and essential thrombocytopenia. *A. Piney*

2871. **Clinical Features, Cytodiagnosis, and Therapy of Multiple Myelomatosis.** (Клиника, цитодиагностика и терапия миэломной болезни (болезни рустицкого))
G. A. Alekseev. Терапевтический Архив [*Terap. Arkh.*] **21**, No. 2, 62–77, March–April, 1949. 6 figs., 30 refs.

Myelomatosis is a systemic disease of the bone marrow. Cytological study of the bone marrow obtained by sternal puncture in a case of myelomatosis shows that there is only one morphological picture and not six different types as has previously been suggested. All myelomata are reticulo-plasmocytomata. The clinical picture is characterized by a classical triad of symptoms: (1) affections of the bones (pain, swelling, and fragility of the bones); (2) changes in the blood (anaemia and occasionally a leukaemia); (3) affection of the kidneys (Bence-Jones proteinuria). To this must be added a fourth sign, a hyperproteinaemia which causes thirst, dryness of the tongue, and a definite oliguria often amounting to anuria. The development of uraemia in a myelomatous kidney is due to an occlusion of the urinary tubules by pathological protein bodies associated with a low blood pressure. As a proteinosis myelomatosis may be compared with a lipoidosis (Gaucher's disease) or a xanthomatosis (Niemann-Pick disease). As a systemic disease myelomatosis resembles a leucosis.

Cytological examination of the bone marrow will lead to a correct diagnosis in 100% of cases. There is no effective treatment of myelomatosis. Reports of successful treatment with antimony and other preparations, described in the literature outside Russia, need verification. A temporary clinical improvement may be achieved by rest, by application of extension to diseased bones, by *x*-ray therapy, and by blood transfusion.
H. W. Swann

2872. **Megaloblastic Bone Marrow in Liver Disease**
E. R. Movitt. *American Journal of Medicine* [*Amer. J. Med.*] **7**, 145–149, July, 1949. 2 figs., 10 refs.

HODGKIN'S DISEASE

2873. **The Treatment of Hodgkin's Disease with Nitrogen Mustard.** (La terapia del linfogranuloma maligno con bis-beta-cloroetilmetil-amina cloridrato)
E. Storti, A. Allegri, and M. Mocchi. *Haematologica* [*Haematologica*] **33**, 149–212, 1949. 18 figs., 26 refs.

A course of nitrogen mustard, 4 to 6 doses on alternate days, the dose being 0·1 mg. per kg. of body weight, was given to 11 patients with Hodgkin's disease, 1 with lymphosarcoma, and 2 with carcinoma of the lung. In 10 cases of Hodgkin's disease the pyrexia, pain, and swelling of the affected lymph nodes subsided fairly well, but these induced remissions were mostly shorter than those observed in cases treated with radiotherapy. In all patients the number of leucocytes, and in particular of neutrophils, fell markedly during treatment. The erythrocyte counts were not influenced except in one case. In the bone marrow the number of myeloid cells fell to about a third and the number of mitoses decreased. The cells obtained by lymph-node puncture showed degenerative changes and especially vacuolation of the cytoplasm.
E. Neumark

2874. **The Clinical Effect of Nitrogen Mustard on Hodgkin's Disease**
L. A. Erf and R. D. Bauer. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **19**, 372–380, April, 1949. 2 figs., 20 refs.

Forty-three patients with proven Hodgkin's disease were treated with methyl bis-(β-chloroethyl)amine; of these 27 had received previous *x*-ray treatment and 13 were resistant to irradiation; in 16 no *x*-ray therapy had been given. The results of treatment with nitrogen mustard were as follows:

	No Improvement	Minimum Improvement	Remission for Less than 6 Weeks	Remission for More than 6 Weeks
Previous irradiation effective	0	4	5	5
Resistant to *x* rays	2	3	5	3
No previous irradiation	0	3	4	9

Three patients developed severe leucopenia, but recovered after transfusion.

The clinical response is apparently due to reduction in size of affected lymph nodes, or of deposits in other tissues, by massive cellular lysis. In addition, relief of pain, fever, and itching occurs in about half the patients in whom these were present. The response is best after the first course, and becomes progressively less satisfactory in later courses. Nitrogen mustard is considered the treatment of choice in generalized or in radio-resistant Hodgkin's disease. *G. Discombe*

2875. **Myelokentric Acid and Lymphokentric Acid in Hodgkin's Disease.** [In English]
F. R. Miller and D. L. Turner. *Acta Haematologica* [*Acta haematol., Basel*] **2**, 78–86, 1949. 7 figs., 9 refs.

2876. **A Case of Hodgkin's Disease Successfully Treated with Male Sex Hormone Associated with Amino-acids.** (Sur un cas de maladie de Hodgkin traité avec succès par l'hormone mâle associée aux acides aminés)
P. Brocq and A. Sluczewski. *Bulletin de l'Académie Nationale de Médecine* [*Bull. Acad. nat. Méd., Paris*] **133**, 461–466, June, 1949.

See also Section Pathology, Abstract 2769.

Respiratory Disorders

2877. **The Treatment of Head Colds with an Antihistamine Drug**
H. G. MURRAY. *Industrial Medicine* [*Industr. Med.*] **18**, 215–216, May, 1949.

The similarity between the early stages of acute coryza and hay-fever and the good response of the latter to antihistamine drugs prompted this investigation. In a factory in Massachusetts, 510 people who reported within the first 24 hours of the onset of a head cold were treated with " pyribenzamine hydrochloride " in 50 mg. doses at 4-hourly intervals. Of these only 5 had had any previous allergic manifestations. Of 494 persons followed up none had had the tablets for more than 3 days and some had been cured by only 2 tablets; 110 reported complete cure within 24 hours. In a further 204 cases the cold was of shorter duration than the ones they had had previously, and symptoms were milder. In 83 there was only some slight improvement in severity and duration, and 97 reported no improvement. Unpleasant side effects occurred in 22 persons, the most common being dizziness and drowsiness. All these were in the group which was not benefited by treatment at all. Only 7 people lost time from work. The author suggests that similar results could be obtained with any other reputable antihistaminic drug. *Marianna Clark*

2878. **Inhalation of Stomach Contents**
A. WILLCOX. *Lancet* [*Lancet*] **1**, 438–439, March 12, 1949. 2 figs., 4 refs.

Two patients inhaled their vomit during recovery from anaesthesia and each, after 2 or 3 hours, developed acute pulmonary oedema and bronchial spasm. The clinical picture was very like that of acute poisoning with chlorine or phosgene, and it is probable that the acid in the gastric juice acted as a similar lung irritant. It is recommended that when such inhalation of vomit occurs immediate bronchoscopic aspiration or postural drainage should be carried out; once pulmonary oedema has developed, however, such procedures may be dangerous, and administration of oxygen and antispasmodics and prophylactic chemotherapy are indicated.
John Forbes

2879. **The Pulmonary Complications of Dysphagia**
J. R. BELCHER. *Thorax* [*Thorax*] **4**, 44–56, March, 1949. 4 figs., 34 refs.

This is a study of pulmonary aspiration phenomena in association with mechanical dysphagia, caused usually by achalasia of the cardia or a pharyngeal diverticulum. The term " dysphagia pneumonitis " is applied to the syndrome. The author reviews a series of 38 cases taken from the literature and has added 9 further examples. Conflicting evidence on the frequency of the association is quoted. In one group of 349 patients suffering from diverticula 8 were found to have developed lung abscess.

Aspiration depends upon the occasional reflux to the glottis level of retained oesophageal fluid in the presence of a dulled cough reflex. Carcinoma of the upper third of the oesophagus produces these conditions with particular efficiency. With obstruction elsewhere recumbency is the most potent factor. An incompetent cricopharyngeal sphincter may play a part. The cough reflex may be impaired by sleep or anaesthesia.

Pulmonary lesions observed included lung abscess 18, bronchiectasis 6, fibrosis 10, lipoid pneumonia 4, pneumonitis 8, and collapse 2. The author points out that the aetiology of all is fundamentally the same. Pulmonary abscess is the most readily diagnosed. It occurs at the sites most liable to bronchial embolism and is thought to be due to a major spill-over of oesophageal contents. Pneumonitis presumably follows small repeated aspirations, fibrosis a prolonged exposure to small aspirations, and lipoid pneumonia a similar assault by oesophageal material of high fat content.

Clinically there are 3 points of particular importance. (1) In 18 of the cases reviewed the presenting symptoms were predominantly respiratory, and in 8 of these the dysphagia was " silent ", that is unappreciated by the patient. (2) Lung lesions may also only be recognized on radiography. (3) In 6 of the 47 cases acid-fast bacilli found in the sputum were proved to be non-pathogenic.
I. McD. G. Stewart

2880. **Administration of Streptomycin by Way of the Pulmonary Lymphatics.** (La streptomicina attraverso i linfatici polmonari. Primi tentativi)
A. SCARPA. *Riforma Medica* [*Rif. med.*] **63**, 25–28, Jan. 15, 1949. 11 figs., 18 refs.

The author demonstrated in living rabbits that dyes injected into the subpleural lymphatics, either through the chest wall or at thoracotomy, rapidly passed into the parenchyma of the lungs and through to the hilum. He applied these findings to the treatment of pulmonary tuberculosis by injecting streptomycin through the chest wall in patients with adherent pleura, 2 to 5 ml. of a 10% solution of streptomycin in physiological saline being injected daily into the subpleural zone of the lung at the level of the lesion and treatment being continued for 2 to 3 months. No ill effects occurred apart from a slight burning sensation at the moment of injection. Of 5 patients, in 2 with apical disease awaiting thoracoplasty and with contralateral bronchopneumonic or nodular infiltration, the contralateral lesions cleared up within 2 months. In 1 patient bilateral apical haematogenous lesions showed rapid resolution with injections of 0·4 g. streptomycin locally daily. In 2 with persisting activity after thoracoplasty the condition became quiescent after 2 months' local treatment.

It is emphasized that this is a preliminary report, without controls, and that fuller details, with follow-up results, will be published later. This route for the administration of streptomycin is worthy of consideration because of the high concentrations that can be obtained locally. *E. G. Sita-Lumsden*

2881. **The Topical Treatment of Lung Abscess**
W. E. BURNETT, G. P. ROSEMOND, H. T. CASWELL, J. H. HALL, and R. M. BUCHER. *Pennsylvania Medical Journal* [*Penn. med. J.*] **52**, 719–725, April, 1949. 5 figs., 12 refs.

Thirteen patients with acute lung abscess were treated by intracavitary instillation of antibiotics through an 18-gauge needle inserted into the abscess cavity under local analgesia and fluoroscopic control. As much as possible of the contents was aspirated, and 1 to 5 ml. of a solution containing 100,000 units of penicillin and 1 g. of streptomycin with a wetting agent was injected. The procedure was repeated every 1 to 3 days for as long as it was possible to locate a cavity. Penicillin was administered intramuscularly in doses of up to 600,000 units daily, and in some cases antibiotics were also inhaled. All the patients had failed to respond satisfactorily to the usual conservative measures. Nine patients rapidly improved and required no additional treatment; 4 improved but later required lobectomy or excision. Pneumothorax occurred in only one case, but was not followed by infection of the pleural space. Infection of the needle track did not occur in any of the cases. Profuse haemorrhage was encountered on one occasion. The authors are impressed by the results obtained, and suggest that the method might be more widely used, but add the warning that it should be undertaken only by competent thoracic surgeons. *J. R. Bignall*

2882. **Involvement of the Lung in Rheumatic Fever.** (Sobre la participación del pulmón en la fievre reumática)
R. ESTRADA GONZÁLEZ. *Archivos del Hospital Universitario, Habaná* [*Arch. Hosp. univ., Habana*] **1**, 75–147, March–April, 1949. 13 figs., 43 refs.

An analysis is made of 17 fatal cases of rheumatic fever, in 6 of which interstitial pneumonia was present. The clinical and morbid anatomical findings are discussed in relation to the literature and the classification suggested by Griffiths and his co-workers is adopted. The difficulty of diagnosis, in the absence of cardiac and articular symptoms, is stressed and it is suggested that differentiation from primary atypical pneumonia can only be made by tests for antistreptolysin and cold agglutinins. *George Hickie*

2883. **Present Status of Aluminum in the Therapy and Prophylaxis of Silicosis**
E. W. BROWN and W. V. WINKLE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **140**, 1024–1029, July 23, 1949. 18 refs.

See also Section Hygiene and Public Health, Abstracts 2661, 2663.

2884. **Clinical and Radiological Observations on the Development and Course of Pneumonic Foci in " Healthy " Subjects.** (Клинико-рентгенологические наблюдения за развитием и течением пневмонических фокусов у " здоровых " лиц)
I. E. KOCHNOVA. Проблемы Тлберкулеза [*Probl. Tuberk.*] No. 2, 15–20, March–April, 1949. 3 figs.

In this article the author reports 14 cases in which, in the absence of any subjective or objective symptoms or signs of pulmonary disease, it was possible to demonstrate radiographically evanescent shadows in the lungs. These disappeared completely in a time varying from 2 to 20 days. No changes in the blood were observed, except eosinophilia in one case. Some of these patients were observed in the course of routine examinations, or examinations for non-pulmonary conditions.

The author discusses the origin of these " fleeting shadows " and concludes that they are due to collapse of localized groups of alveoli due to complete or partial obstruction of the smaller bronchioles. She considers that in some cases such temporary collapse may be followed by spontaneous re-inflation (as in these 14 cases) whereas in others such a condition may form a basis for the development of pneumonic processes.

[In *A Practical Manual of Diseases of the Chest*, 1948, pp. 625–639, Davidson refers to a similar phenomenon; in most of the cases he describes, however, the periods during which they were observed were longer, and in several of the patients previously negative Mantoux tests in a dilution of 1 in 10,000 became positive after the disappearance of the shadow. Also none of these patients was entirely symptom free. The possibility that allergy is the cause of such phenomena as are described in this article cannot be disregarded, in spite of the rare occurrence of eosinophilia.]
L. Firman-Edwards

2885. **The Control of Experimental Pneumonia with Penicillin. III. Inhalation Therapy of Established Pneumonia, as Related to Blood and Lung Levels**
C. E. WILSON, S. H. DURLACHER, and E. A. BLISS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **95**, 509–514, April, 1949. 5 refs.

The exposure of rats with pneumonia induced by intrabronchial instillation of a mucin suspension of pneumococci to aerosols containing 400 units of penicillin per litre of air reduced the mortality by at least 75%. Intramuscular injections of penicillin were not so effective, despite the fact that blood penicillin levels were much higher than those found after aerosol treatment. Approximately three times as much penicillin was recovered from the lower respiratory tract (lungs, bronchi, and trachea) of normal animals similarly exposed as was recovered from the same tissues of the pneumonic rats. Moreover, whereas in normal rats the amount of penicillin deposited in the trachea was only a small fraction of the total recovered from the lower respiratory tract, in pneumonic rats the proportion was much higher and there was only a trace of penicillin in the consolidated parts of the lung. Nevertheless, the pneumonic rats

had 25 times as much penicillin in their lungs and trachea after inhalation as after intramuscular injection. In both normal and pneumonic rats appreciable amounts of penicillin persisted in the lung one hour after inhalation.

G. B. West

2886. **The Skin Reaction with Polysaccharide in Lobar Pneumonia.** (Кожная реакция с полисахаридом при крупозной пневмонии)

L. P. ELMANOVICH. Клиническая Медицина [*Klin. Med., Mosk.*] **27**, No. 5, 65–68, May, 1949. 7 refs.

This article records the results of cutaneous reactions to the capsular polysaccharides of various types of pneumococci in 60 cases of lobar pneumonia. The proportions of the different types were: type I, 52%; type II, 17%; type III, 6%; group IV, 25%. The polysaccharides used were prepared from the capsules of types I and III pneumococci. All infections due to other types gave negative results. These reactions are strictly specific and are therefore of diagnostic importance.

Positive reaction to the specific polysaccharide reflects a good reactivity and is of good prognostic omen; reactions appear from the 4th day of the disease, reach their maximum on the 9th day, and persist up to the 42nd day. Negative results in cases of infection with the corresponding type are of bad omen.

The method was introduced by Francis in 1933. The technique consists in the subcutaneous [intracutaneous?] injection of 0·1 ml. of a 1 in 10,000 solution of the specific polysaccharide into the flexor aspect of the forearm. The reaction appears within 1 hour (often in 20 minutes) and consists of a vesicle surrounded by an erythematous areola, which dies away in 1 to 2 hours. Neither this nor the serum-agglutination type reaction is affected by sulphonamide treatment. Several typical observations are described in detail. The simplicity and reliability of the test, and the speed with which a response is obtained, make it a valuable addition to clinical laboratory methods.

L. Firman-Edwards

2887. **Pulsus Paradoxus and Pleurisy**

W. E. GIBB. *British Journal of Tuberculosis* [*Brit. J. Tuberc.*] **43**, 1–6, Jan., 1949. 15 refs.

The author describes the history of pulsus paradoxus since it was first recognized in a patient with a thickened pericardium by Lower in 1669. Greisinger (1854) noted that the cervical veins were distended on inspiration in patients with chronic mediastino-pericarditis and postulated that the mediastinal adhesions caused narrowing of the superior vena cava and large veins when the thoracic cage increased in size on inspiration. In pericardial effusions the pulsus paradoxus is due to the raised intrapericardial pressure and is abolished by aspiration of the fluid, and Fletcher (1945) showed that there is a marked fall in right intra-auricular pressure after the pericardial effusion is tapped.

Williams (1907) noted that pulsus paradoxus was common in normal school-boys and ascribed this to the pooling of the blood in the pulmonary vessels with deep inspiration. Crowden and Harris (1929) observed that in Müller's experiment (an attempt after expiration to inspire with a closed glottis) the right auricle and pulmonary vessels enlarged, while the arterial pulse disappeared; this is due to increase in the reservoir of blood in the lungs. In Valsalva's experiment (after inspiration, an attempt at forced expiration against a closed glottis) the heart is diminished in size, the cervical veins are engorged, and the increase in intrapleural pressure by impeding the venous return to the heart causes a fall in ventricular output with absence of the arterial pulse.

Wenckebach described three clinical types of pulsus paradoxus. (1) The mechanical type, due to mediastino-pericardial fibrosis in which the great vessels are further obstructed during inspiration by the pull of adhesions. (2) The extrathoracic type, due to compression of the subclavian artery between the first rib and the clavicle and which can be artificially produced in normal subjects. This is not true pulsus paradoxus, as all peripheral arteries are not affected. (3) The dynamic type, in which changes in the intrathoracic pressure during respiration cause variation of pulse volume. This type is seen with respiratory embarrassment and has been found in tracheal or bronchial stenosis, bronchial spasm, pneumonia, and emphysema and occasionally in pleurisy, myocardial failure, and severe haemorrhage. It has also been found immediately after pneumonectomy.

The author describes 2 cases of pleurisy with massive effusion, one on the right and the other on the left side, in which respiratory embarrassment and pulsus paradoxus were present; after paracentesis the symptoms and pulsus paradoxus disappeared. There was no evidence of pericarditis and he concludes that the underlying collapse of the lung on the affected side, together with the increased intrapleural pressure, caused an over-filling of the right heart and a diminished return of blood to the left side of the heart.

J. L. Livingstone

2888. **The Diagnostic Problem of Primary Pleural Effusions**

J. R. KRAFT. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **59**, 259–269, March, 1949. 18 refs.

In 100 cases of primary pleural effusion the patient was kept under observation for a minimum of 6 months; 90% of the patients were aged 18 to 30; 14 negroes and 7 Japanese Americans were included. All had positive tuberculin tests. In 18 of 51 specimens of pleural fluid the presence of tubercle bacilli was demonstrated by guinea-pig inoculation; of 30 tested by culture only, 2 were positive; 9 were positive by both methods. In 3 cases a second pleural effusion appeared 2 to 4 months after the onset of the first; one of these 3 patients later developed tuberculous peritonitis and finally tuberculous meningitis. In 21 out of the 100 cases a parenchymal lesion was detected radiologically 2 to 10 months after the onset of the effusion. All except 3 of these patients were still in bed.

[This paper confirms the findings of others that, even since the seriousness of primary pleural effusion has been appreciated, 20 to 30% of cases develop other clinical manifestations of tuberculosis within 3 to 5 years.]

John Crofton

Digestive Disorders

2889. **The Secretin Test of Pancreatic Function and its Use in Steatorrhoea.** [In English]
J. NEWSOME. *Gastroenterologia* [*Gastroenterologia, Basel*] **74**, 257–269, 1949. 5 figs., 24 refs.

An unusually full and careful description is given of the type of tube used by the author for duodenal intubation and the method of passing it. It was not found possible to prepare suitable secretin so that the expensive Swedish " pancreotest " had to be imported. Five tests were carried out on normal controls, of which 3 were failures, and 7 tests were carried out on patients with a provisional diagnosis of tropical or non-tropical sprue (one failure). The results conform to those published by other workers. The effect of the test was to change the diagnosis in 2 patients from idiopathic steatorrhoea to chronic pancreatitis. Further clinical evidence was found to support this change of diagnosis. *Denys Jennings*

STOMACH

2890. **Effect of Dialyzed Enterogastrone upon Twelve-hour Nocturnal Gastric Secretion in Man**
J. B. KIRSNER, E. LEVIN, and W. L. PALMER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 685–688, April, 1949. 9 refs.

The effect was investigated of intramuscular injections of a recent preparation of enterogastrone free from inactive protein on the 12-hour nocturnal secretion of 10 patients with peptic ulcer. Doses of 200 to 2,000 mg. were ineffective. However, of the 6 patients who received 5,000 mg., in 5 there was a pronounced and in 1 a moderate decrease in the concentration of free hydrochloric acid. In addition, the volume was decreased in 3 cases. The authors do not consider that the present preparation warrants further clinical trial, as injections are very painful, the effect is only temporary, and enormous doses are required. *R. Schneider*

2891. **The Effect of Urine Extract from Oöphorectomized Dogs on Gastric Secretion**
J. KAULBERSZ, T. L. PATTERSON, D. J. SANDWEISS, and H. C. SALTZSTEIN. *Review of Gastroenterology* [*Rev. Gastroent.*] **16**, 254–256, March, 1949. 2 refs.

It has previously been demonstrated that an extract can be prepared from the urine of normal dogs which inhibits the gastric secretion of dogs into which it has been injected. In the present investigation, a comparable extract prepared from the urine of bitches subjected to oöphorectomy was tested in 41 " double histamine " experiments on 4 dogs with a gastric fistula and 5 dogs with a Heidenhain pouch. Histamine diphosphate was injected subcutaneously in doses of 0·5 or 1 mg., and the total output of hydrochloric acid during 70 minutes following the injection was measured; the histamine injection was repeated after an interval of 3 hours. The extract was given intravenously, mostly in 2-mg. doses, 10 minutes before either the first or the second injection of histamine; the gastric secretory response to the histamine given alone acted as a control of the response to extract and histamine together.

Results showed that the extract did not consistently inhibit gastric secretion, nor did it have a delaying effect. The authors conclude that extracts from the urine of bitches from which the ovaries have been removed contain little or no " urogastrone ", and suggest that the ovaries may have some influence on the production of this substance, either directly or, more probably, through the pituitary gland. It has previously been reported that the extract from the urine of dogs subjected to hypophysectomy produces a much delayed inhibitory effect on gastric secretion as compared with the extract from normal urine. *Joseph Parness*

2892. **The Effect of Urine Extract from Thyroidectomized Dogs on Gastric Secretion**
J. KAULBERSZ, T. L. PATTERSON, D. J. SANDWEISS, and H. C. SALTZSTEIN. *Review of Gastroenterology* [*Rev. Gastroent.*] **16**, 257–259, March, 1949. 6 refs.

Urine was collected from 6 bitches 1 to 3 weeks after the thyroid gland had been removed, care having been taken to preserve the parathyroids. The extract prepared from the urine was injected into dogs with gastric fistula or Heidenhain pouch in doses of from 2 to 5 mg. in 47 " double histamine " experiments. This resulted in a more pronounced inhibition of gastric secretion in the period immediately following injection of both extract and histamine than after the injection of histamine alone. The inhibitory effect was similar to, and at least equal to, that produced by the " urogastrone " of normal urine ; there was no delayed inhibitory effect. It has previously been reported that an extract prepared from the urine of bitches which have had both the thyroid and the ovaries removed also contains the inhibitory substance in approximately normal quantity.
Joseph Parness

2893. **Development of the Nervous Phase of Gastric Secretion in Sensitized Dogs.** (О развитии нервной фазы желудочной секреции у аллергизированных собак)
C. G. GENES and N. G. LESNOI. Архив Патологии [*Arkh. Patol.*] **11**, No. 1, 22–25, Jan.–Feb., 1949. 4 refs.

Horse serum was used to sensitize dogs which were previously subjected to a gastrostomy and oesophagostomy. Sham feeding of such animals showed that the amount of gastric juice secreted during the nervous

phase was decreased. Its acidity and digestive qualities remained unchanged. Desensitization was accompanied by a return to normal of the gastric juice level. It is suggested that sensitization leads to inhibition of the secretory fibres of the vagus. *L. Crome*

2894. **The Role of Pathological Irritation in Disturbances of Gastric Secretion (in Sham Feeding).** (О роли патологического раздражения в расстройстве секреции желудочного сока)
S. I. Frankstein and N. N. Lebedev. Архив Патологии [*Arkh. Patol.*] **11**, No. 1, 31–34, Jan.–Feb., 1949. 1 fig., 8 refs.

Dogs were prepared by a preliminary induction of gastrostomy and oesophagostomy, and a local burn was then inflicted on the gastric mucosa. Sham feeding in these circumstances showed that gastric secretion was at first greatly reduced, and that this was succeeded in 24 hours by a period of hypersecretion. The hypersecretion was present during both the nervous and the hormonal phases of secretion. *L. Crome*

2895. **The Action of Thephorin upon Histamine-induced Gastric Secretion in Dogs and on Gastric Ulcer Formation in Rats**
G. Lehmann and P. L. Stefko. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 372–379, March, 1949. 3 figs., 25 refs.

The volume, free hydrochloric acid content, and *p*H of gastric juice secreted by a Heidenhain pouch in bitches were determined after the subcutaneous injection of 0·1 or 0·025 mg. histamine phosphate per kg. of body weight 30 minutes after a similar injection of 20 mg. " thephorin " per kg. [Thephorin is 2-methyl-9-phenyl-2 : 3 : 4 : 9-tetrahydro-1-pyridindene.] A reduction of 30% in volume and in quantity of free hydrochloric acid was found irrespective of the dose of histamine, but no change occurred in the *p*H. This represents a 75% inhibition of histamine action. Intramuscular injection of 60 mg. histamine phosphate per day into rats resulted in a 90% incidence of gastric ulcers; this was reduced to 13% if the histamine injection was followed after 5 hours by 20 mg. thephorin per kg.; treatment with 10 mg. atropine per kg. had no effect. Thephorin (20 mg. per kg.) almost completely prevented the appearance of gastric ulceration in Shay rats in which the pylorus had been ligated, lower doses having proportional effect. Atropine in a dose of 10 mg. per kg. has a similar effect to 10 mg. thephorin per kg. It is suggested that the effect of thephorin is equivalent to that of vagotomy. *J. Dawson*

2896. **Clinical Aspects of Prolapsed Gastric Mucosa**
F. W. Wilson and W. H. Granger. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **16**, 129–131, April, 1949. 2 figs., 11 refs.

In this paper the authors consider a rare but interesting phenomenon of gastric pathology, namely, prolapse or herniation of redundant gastric mucous membrane through the pylorus. Of 10,500 general admissions to the U.S. Veterans Administration Hospital, McKinney, Texas, the condition was diagnosed 25 times, the incidence being 0·24% of all general admissions and 1·0% of 2,511 *x*-ray examinations of the upper alimentary tract. The cause is discussed and various hypotheses are cited, the authors being inclined to believe that there is some individual predisposition to prolapse from an anatomical standpoint, since 7 of their 25 cases showed other abnormalities of the stomach; these consisted of hiatus hernia (4 cases), cascade stomach (1), high transverse stomach (1), and gastric ulcer (1). They believe that a disturbance of nerve function may be a predisposing factor.

An analysis of symptoms leads to the conclusion that the diagnosis cannot be made on clinical grounds, the symptoms being those of a non-specific disturbance of gastric function (apart from severe gastro-intestinal bleeding which was present in 7 patients). Radiological examination is essential for diagnosis, the characteristic findings being: (1) a typical deformity of the duodenal bulb by the mushroom-shaped mass of mucous membrane; (2) the presence of redundant mucosal folds in the pyloric canal; (3) absence of irritability of the duodenal bulb; (4) increased gastric peristalsis; and (5) absence of gastric dilatation. An attempt in 3 cases to reduce the prolapse by direct pressure during *x*-ray screening was unsuccessful. Partial gastrectomy or excision of the redundant folds has been recommended and is indicated for severe recurrent haemorrhage or vomiting, but the authors' patients responded satisfactorily to ordinary medical treatment for peptic ulcer. *T. L. Hardy*

2897. **Studies of Gastric Function by Direct *p*H Determination in the Stomach.** (Untersuchungen der Magenfunktion durch direkte *p*H-Bestimmungen im lebenden Magen)
H. Kreitner and M. Pantlitschko. *Wiener Zeitschrift für Innere Medizin* [*Wien. Z. inn. Med.*] **30**, 160–167, April, 1949. 3 figs.

The usual methods of determination of hydrochloric acid and acidity in the gastric juice are reviewed and critically appraised. It is held that none of the routine methods yields very accurate results, particularly as regards the end-point titration. The authors designed and constructed an apparatus (which is described and illustrated) for direct *in vivo* electrometric determination of *p*H of the gastric juice by means of an antimony electrode (combined with a calomel electrode) fitted into a modified duodenal sound. The technique of electrometric determination of *p*H of the gastric juice is described in detail; the *p*H values so obtained (after an injection of histamine) *in vivo* are compared with the values obtained by routine methods (after ingestion of 300 ml. of 5% alcohol on an empty stomach). The titration values obtained by routine methods were somewhat higher (as expected) than those determined electrometrically. Typical *p*H values were obtained for the gastric juice of subjects suffering from gastric and duodenal ulcer and gastric carcinoma. Experiments were inaugurated to

test the suitability of electrometric *p*H determination for ascertaining the reaction of the renal pelvis and for observing the effect of various drugs on the secretion of gastric juice. *H. P. Fox*

2898. **Acid-neutralizing Power of Several Protein Hydrolysates and Other Substances used in Ulcer Therapy**
S. M. SAMIS and F. HOLLANDER. *Gastroenterology* [*Gastroenterology*] **12**, 665–670, April, 1949. 2 figs., 5 refs.

The authors investigated the neutralizing power of four commercial preparations of protein hydrolysate and compared it with that of fresh milk, aluminium gel, and sodium bicarbonate. Three of the protein hydrolysates were found to have sufficient neutralizing power to be effective antacids when taken in a dose of 300 g. distributed throughout the day.

Christopher Hardwick

2899. **The Hydrochloric Acid Test in Ulcer Diagnosis.** (Die Salzsäureprobe in der Ulcusdiagnostik)
G. GOTTSEGEN and B. HERMANN. *Gastroenterologia* [*Gastroenterologia, Basel*] **74**, 270–279, 1949. 5 refs.

[Pickering (*Clin. Sci.*, 1946, **6**, 63) showed that the introduction of 200 ml. of N/10 hydrochloric acid reproduced ulcer pain in 20 out of 23 patients and that the pain could be abolished by replacing the acid with weak alkali. No pain was caused by an equivalent amount of normal saline. Since 2 of the 3 failures could be explained the test appeared valuable. It was in fact used in the U.S.A. during the war on soldiers suspected of exaggerating their symptoms.]

The present paper describes the routine use of this test immediately after the test-meal and before withdrawing the tube. In 400 control patients it was negative, that is, the acid caused no pain. In 14 out of 29 cases of gastric ulcer and 56 out of 89 cases of duodenal ulcer, however, the response was also negative. No explanation could be found for these failures. They were not related to the size of the ulcer, to its duration, or to the finding of a positive benzidine reaction in the faeces. Patients with hypoacidity were rather more liable to feel pain after the introduction of the acid than those with hyperacidity. On 33 patients the acid test was repeated after 6 weeks' in-patient treatment. In 18 out of 33, a previously positive response became negative and the ulcer crater disappeared. In 7 cases the test remained positive, and in 5 of these the crater could still be demonstrated. In 7 cases a previously negative response remained negative and only in 1 of these 7 did the ulcer crater and pain persist. In 1 case a previously negative response became positive and the ulcer crater increased in size. The trend of the results thus fits in with expectation, but the large number of exceptions provide an interesting theoretical puzzle.

[This is an important paper. Pickering's results are open to criticism in so far as they refer to the small minority of really severe patients with ulcer whose pain persists after treatment in hospital. In many patients pain is associated with motor dysfunction, and in some of these it is possible that the ulcer is the result of the functional disorder and not the cause of it. If we admit, as we must, that ulcers can persist without causing pain and that these ulcers are insensitive to the acid test, we must admit that such ulcers could be associated with a painful functional disorder of motility.]

Denys Jennings

2900. **Cytohistologic Diagnosis of Material Aspirated from Stomach. Accuracy of Diagnosis of Cancer, Ulcer and Gastritis from Paraffin-embedded Washings**
H. L. RICHARDSON, F. B. QUEEN, and F. H. BISHOP. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **19**, 328–340, April, 1949. 5 figs., 23 refs.

The deposit of gastric washings obtained after an alcohol–histamine meal was fixed in picro-formol, embedded, sectioned, and stained with haematoxylin-orange G-eosin. In normal stomachs squamous cells predominate, with some cubical or columnar epithelium in which small, deeply staining nuclei are present. In gastritis, large strands of mucosa infiltrated with leucocytes appear. In cancer the cells have large, deeply staining nuclei, usually containing prominent nucleoli; the cytoplasm is scanty, vacuolated, with ill-defined boundaries. Ulcers yield a fibrin mass containing leucocytes.

Out of 78 cases examined (27 of cancer, 24 of gastric ulcer, 9 of gastritis, and 18 controls), a correct diagnosis was obtained in 13 cases of cancer, 20 of ulcer, and 6 of gastritis, and in 11 normal subjects. Two false-positive diagnoses of cancer in patients with ulcer or gastritis were made.

[This is an important paper, and should be read by all concerned with the diagnosis of these diseases.]

G. Discombe

2901. **Hog-Stomach Extract and Casein Hydrolysate in Peptic Ulcer**
A. W. KAY, R. A. JAMIESON, and W. E. SMITH. *British Medical Journal* [*Brit. med. J.*] **1**, 519–520, March 26, 1949. 5 refs.

An experimental method designed to eliminate the variations due to spontaneous remissions was used to investigate the effect of "pepsac" (a hog-stomach extract) and "casydrol" (casein hydrolysate) in peptic ulcer. The test substance was administered for 3 months and then withheld for 3 months, the sequence being then repeated without reference to the symptoms. In this way two test periods and two control periods were obtained. All the patients had proven gastric or duodenal ulcers with an average duration of symptoms of 12½ years. Alkalis were permitted only for severe pain.

In the first trial 30 g. pepsac was given thrice daily to 41 patients. In 9 there was improvement as regards either the severity or the duration of attacks, but the remainder either did not improve or failed to complete the trial. There was thus no evidence that pepsac contains an anti-ulcer factor. In the second experiment casydrol was given to two groups of patients. Sixteen were given a tablespoonful thrice daily; all gained

weight but only in 2 was there any improvement in dyspepsia. In 7 patients the above method of trial was abandoned and they were given hourly feeds exclusively of casein hydrolysate, to a total of 600 g. daily for 7 days. Again there was a gain in weight in all cases but no constant improvement in dyspepsia.

E. G. Sita-Lumsden

2902. **Influence of Ultraviolet Irradiation on Gastritis and Peptic Ulcer.** (Влияние ультрафиолетовых облучений при гастрите и язвенной болезни)
G. B. KATSNELSON. Клиническая Медицина [*Klin. Med., Mosk.*] **27**, No. 2, 81–85, Feb., 1949.

The author treated by ultraviolet irradiation the following series of cases: gastric ulcer, 13 cases; duodenal ulcer, 41; "periduodenitis", 4; "pyloroduodenitis", 4; and "gastritis", 38. Two cases are described in detail. [In no case is the evidence for the diagnosis mentioned, other than some slight reference to the symptoms. Diagnostic radiology is nowhere referred to.] The patients received treatment monthly for 10 to 12 months. At each attendance they received just sufficient irradiation to cause erythema. The irradiated area was at first confined to the lower abdomen, but later the spinal region (C5 to T2 and T7 to 9) was also irradiated. It is said that in 71% of patients there were "positive clinical results". Blood complement titre was low in patients suffering from "gastritis" and gastric ulcer. The titre increased during treatment correspondingly with the clinical improvement.

[There is insufficient evidence for the diagnoses, the true significance of some of which (for example, pyloroduodenitis) is far from clear. The criteria of clinical improvement are not stated. The results are inadequately presented for critical assessment.] *Jeffrey Boss*

2903. **The Influence of Smoking upon the Management of the Peptic Ulcer Patient**
R. C. BATTERMAN and I. EHRENFELD. *Gastroenterology* [*Gastroenterology*] **12**, 575–585, April, 1949. 30 refs.

The authors investigated the effect of smoking on the response to treatment of 108 ambulant patients with peptic ulcer. Fifty-six were smokers, and 43 of these continued to smoke throughout the investigation. Twenty-six had been smokers but had stopped; 13 of these resumed the habit when clinical improvement occurred. Non-smokers numbered 39. Of the smokers, a satisfactory clinical response was obtained in 46·8%; of the non-smokers, satisfactory improvement occurred in 85%. In each of the 26 patients who had stopped smoking of their own accord the response to treatment was satisfactory, but 11 of the 13 who resumed had immediate exacerbations.

In an endeavour to find an alternative cigarette for those patients who responded poorly but who could not give up the habit, the use of processed tobacco in which the nicotine content was only 0·85% was investigated. Of 28 such patients a satisfactory response was obtained in 22. *Christopher Hardwick*

See also Section Radiology, Abstract 2764.

INTESTINES

2904. **A Clinical Evaluation of Diverticulosis of the Colon.**
M. FELDMAN and S. MORRISON. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **16**, 126–128, April, 1949. 5 refs.

The authors investigated 205 cases of diverticulosis of the colon in order to decide whether uncomplicated diverticula cause characteristic symptoms. Apart from diverticulitis in 23 cases there were no other complications. There was a preponderance of males (118 males to 87 females) while 163 cases occurred in patients between the ages of 50 and 80.

The authors were unable to confirm the widely held belief that weight and build are aetiological factors of importance. Of 70 patients so studied 18 were classified as obese, 40 as of medium build, and 12 as slender. They quote the work of other authors to illustrate the differences of opinion held on whether diverticulosis of the colon is productive of symptoms or not; they made a detailed clinical and radiological examination of the patients in their series. The bowel habits showed much variation; 59 patients had normal bowel action, 92 complained of constipation, 15 of alternating constipation and diarrhoea, and 39 of diarrhoea only. Likewise, there was much variation in the type of stool passed. Pain and tenderness were uncommon but the authors record the association of an irritable spastic colon, with diffuse or localized pain, in 130 of their 205 cases. This high incidence they regard as a possible causative factor in the production of symptoms.

In the vast majority of cases (177) the diverticula were multiple and involved the sigmoid and descending colons. Proctoscopic examination revealed a normal rectum. The authors summarize their views by stating that uncomplicated diverticulosis does not, as a rule, produce intestinal symptoms, and that such symptoms as are produced are due to an associated irritable or spastic condition of the colon which may possibly be aggravated by the presence of diverticula.

[The value of this paper lies in its emphasis on abnormal muscular movements of the colon in association with diverticulosis. The authors appear to regard the irritability of the colon as secondary to the diverticula, but there is a good deal of evidence to suggest that the diverticula are themselves the result of localized spastic contraction of the bowel (Edwards, *Proc. R. Soc. Med.*, 1939, **32**, 1495).] *T. L. Hardy*

2905. **Chronic Diarrhoea**
J. W. PAULLEY. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] **42**, 241–244, April, 1949. 28 refs.

Chronic diarrhoea is classified by the author on physiological grounds as due to one or more of the following disturbances of function: (*a*) Inadequate absorption in the small intestine of water and food products, particularly fat, and in the large intestine of water only. (*b*) Excessive secretion of mucus and exudation of serum

and even blood. (*c*) Disordered motility of muscle and increased irritability. A study of 171 cases of ulcerative colitis at the Middlesex, Central Middlesex, and St. Mark's Hospitals, London, revealed that its causation was mainly psychological and that it was the result of stress affecting people with a certain clearly defined personality. These patients showed complete dependence, emotional immaturity, lack of normal adult expression and aggression, deep narcissism, and extreme sensitivity with a tendency to prolonged brooding over real or imagined wrongs or insults. The personality of patients suffering from Crohn's disease, idiopathic steatorrhoea, and, in some cases, chronic amoebiasis was found to be closely related to that of patients with colitis. In those patients with disease involving mainly the small intestine the personality was intermediate between that of the patient with colitis and that of the patient with duodenal ulcer, with less aggression and compensatory striving for security than in the latter.

Functional changes—hyperaemia, mucosal lymphoedema, motor irritability, and chronic inflammation—might be seen on gastroscopy or sigmoidoscopy in many cases of chronic dysfunction of the alimentary tract. These changes persisting for prolonged periods as a result of emotional stress in susceptible persons might well lead to atrophy of the jejunum and impaired particulate fat absorption such as is found in cases of active steatorrhoea, and doubt is expressed about the significance of Thaysen's findings in steatorrhoea. Observations that disease in one part of the alimentary tract is sometimes associated with similar disease in other parts are put forward as further reason for regarding such diseases in relation to the whole gut rather than as isolated conditions. *I. Ansell*

See also Section Microbiology, Abstracts 2796 (*a*)–(*e*) and 2797.

LIVER

2906. **Studies on the Genesis of Liver Necroses on the Basis of Experimental Disturbances of the Circulation.** (Untersuchungen über die Genese von Lebernekrosen auf Grund experimenteller Kreislaufstörungen)
L. H. KETTLER. *Virchows Archiv für Pathologische Anatomie und Physiologie* [*Virchows Arch.*] **316**, 525–574, 1949. 12 figs., 53 refs.

According to the author of this massive article, he has produced several fundamentally distinct forms of hepatic necrosis by mechanical obstruction of afferent or efferent vessels of the rabbit liver. Two forms are specially emphasized, the single-cell necroses (*Einzelnekrosen*) and group necroses (*Gruppennekrosen*). The " single-cell necroses " appear very rapidly, disappear equally rapidly after restoration of the circulation without trace, and may be easily overlooked. They are caused by toxic substances produced by brief but severe portal congestion, and anoxia plays no part in their production. The " group necroses " differ from the anoxic centrilobular necroses, with which they have been generally confused, in that they have a sharp border, are generally situated in the midzone, and involve scattered lobules rather than the whole liver. They are often wedge-shaped or streaky, involving only one sector of the lobule. Their earliest stage is a vacuolar degeneration of the liver cells. They arise through intense capillary dilatation probably of nervous origin, stimulated by acute congestion of the liver, and anoxia has no demonstrable part in their production. In man, group necroses and centrilobular necroses may co-exist. A third form of necrosis, the " net " type (*Netznekrosen*), previously described only in biliary stasis, was also produced by simple vascular obstruction.

[The 103 pages filled by this article and an earlier one on vacuolar degeneration of the liver cells (*Virchows Arch.*, 1948, **315**, 587) do not readily yield much further information. The hepatic vein was clamped in 51 rabbits and the portal vein and hepatic artery in 58 for varying times. Experimental details are meagre and any objective view of the results is extremely difficult to obtain.]
Bernard Lennox

2907. **Roussy's Cirrhosis (Senile Cirrhosis). Its Relation to the Endocrines, with Special Reference to the Parathyroids.** (Cirrhose de Roussy dite cirrhose des vieillards, cirrhose sénile ou cirrhose au début. Ses rapports avec les glandes endocrines et en particulier avec les parathyroïdes)
C. BERDJIS CHAMSI. *Archives des Maladies de l'Appareil Digestif* [*Arch. Mal. Appar. dig.*] **38**, 153–168, March–April, 1949. 7 figs., 15 refs.

This work is reported from the Cancer Institute, Paris, and the Pathology Institute, Geneva. A type of early cirrhosis in old people is referred to as Roussy's cirrhosis. The author [who would appear to ignore much of the recent work done on liver pathology in Great Britain and North America] reviews various classifications of cirrhosis and points out that Roussy's cirrhosis fits into none of these. The condition occurs in people over 60. The clinical signs and symptoms are variable and vague. However, Volhard's test, measurement of the icterus index, and the rose bengal excretion test are sometimes helpful. The disease progresses slowly and there are few complications.

The material discussed consisted of 35 cases from among 2,500 patients at the Cancer Institute, Paris, and 15 cases from Geneva found among 470 cases whose parathyroids were being investigated. The shape and size of the liver are not significant. Fine granulations may be seen on parts or the whole of the smooth surface; they are 1 to 2 mm. apart and the size of millet seeds. On section, the granulations are less obviously brownish-yellow on the usual brownish-red background. The connective tissue round Kiernan's spaces is increased. There is general fine cirrhosis, and the portal spaces seem more numerous; there is some lymphocytic infiltration, and Glisson's capsule is increased in size. The spleen frequently shows perisplenitis, is often enlarged, and is usually indurated, hyperaemic, hyperplastic, and fibrotic. The parathyroids in the commoner types of cirrhosis are usually small, with hyperplasia of clear cells, diminution in the number of oxyphil cells, frequent mast cells, lymphocytic infiltration, and interstitial sclerosis. In

Roussy's cirrhosis the parathyroids were examined in 15 subjects, all of whom had normal bones and kidneys. There were huge numbers of oxyphil cells occupying almost the whole gland, and the clear cells were reduced in numbers. *Peter Harvey*

2908. **Significant Factors in the Causation of Biliary Cirrhosis**
R. C. SCHMITZ and R. P. SINAIKO. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **16**, 121–125, April, 1949. 5 figs., 5 refs.

This is a detailed analysis of 93 cases of biliary cirrhosis discovered during 3,922 post-mortem examinations over a period of 18 years. The main causes were as follows: carcinoma of the pancreas, 28·9%; stones in the common bile duct, 21·5%; carcinoma of the bile duct, 17·4%; and carcinoma of the gall-bladder, 12·9%.

[For detailed statistical data concerning the incidence of the various signs, symptoms, and pathological changes encountered the paper should be consulted in the original.] *R. Schneider*

2909. **Hypervolemic Anemia in Cirrhosis**
J. C. BATEMAN, H. M. SHORR, and T. ELGVIN. *Journal of Clinical Investigation* [*J. clin. Invest.*] **28**, 539–547, May, 1949. 7 figs., 24 refs.

Blood-volume studies by the Evans-blue method have been carried out in 6 cases of cirrhosis of the liver. In 3 of these the blood volume was 20 to 40% above normal. These patients had a low haemoglobin value, but the apparent anaemia could be fully explained by the increased blood volume. Hypochromic microcytic anaemia occurs infrequently in cirrhosis, but generally responds to iron. Normochromic or macrocytic anaemia responds poorly, if at all, to folic acid or liver extract. The failure of such patients to respond to iron or other haematinic therapy is, it is suggested, due to the fact that they had a normal circulating erythrocyte mass.
C. L. Cope

2910. **Vitamin K in the Treatment of Liver Cirrhosis.** (Vitamin K bei der Behandlung der Lebercirrhose)
M. KÜLEY. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **79**, 365–367, April 23, 1949. 1 fig., 15 refs.

The treatment with vitamin K of 15 patients suffering from cirrhosis of the liver is described. The normal daily dose was 40 mg., which was given intravenously for 7 to 10 days, the course being repeated after an interval of 5 to 6 days and the treatment continued for a considerable time. The total dose of vitamin K given was 2,400 to 10,000 mg.

In 7 of the 15 cases treated there was a diuretic response, with diminution of ascites and disappearance of oedema. The blood protein level rose and the albumin-globulin ratio approached normal. Of the remaining 8 patients 2 died of tuberculosis and 6 did not respond to vitamin K treatment. The diagnosis was confirmed in all cases by punch biopsy, but in no case did biopsy performed after treatment show an improvement of the histological state, in spite of clinical improvement. Of 12 control cases, not treated with vitamin K, diuresis occurred only in one patient, and one died. [The 6 case histories attached are less convincing than the paper itself.]
Z. A. Leitner

2911. **Preliminary Observations on the Antidiuretic Substance Recovered from the Urines of Patients with Cirrhosis of the Liver**
G. H. STUECK, S. H. LESLIE, and E. P. RALLI. *Endocrinology* [*Endocrinology*] **44**, 325–332, April, 1949. 4 figs., 18 refs.

The authors describe a method for concentrating the antidiuretic activity in the urine of patients with hepatic cirrhosis. The urine was dialysed, concentrated 40-fold, filtered, and then passed through a permutit column and fractionally eluted with water and acidified sodium chloride solution. The antidiuretic activity present in the sodium chloride eluates of *p*H 4 to 5 persisted when they were kept in the cold for 4 months. As the eluate lost activity on dialysis, there was probably some loss during initial dialysis of the urine. The loss of activity was proportional to the logarithm of the concentration; this does not conform with simple diffusion loss. The eluate lost activity in neutral or alkaline conditions, behaving thus like neurohypophysial antidiuretic factor and not like ferritin. *Peter C. Williams*

2912. **An Experimental Study of the Relationship Between Plasma Proteins and Liver Disturbance**
K. K. CHENG. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **61**, 23–47, Jan., 1949. 7 figs., bibliography.

The author has tested the hypothesis that the liver is the sole or main source of plasma proteins. This was done by producing liver damage and subsequently measuring concentrations of plasma proteins and their fractions. The author used 177 rats and 44 rabbits, and the experimental procedures were carefully controlled. Liver damage was caused (and confirmed histologically) by the following procedures: carbon tetrachloride injection in rabbits (0·5 to 1 ml. per kg. body weight), cutaneous application of coal tar in rabbits (2 ml. painted on twice weekly), feeding of butter yellow to rats (1 g. in 1 kg. of food), ligation of the common bile duct in rats, production of Eck fistula in rats by the technique of Whitaker (*Proc. Soc. exp. Biol., N.Y.*, 1946, **61**, 420), hepatectomy in rabbits by the technique of McMaster and Drury (*J. exp. Med.*, 1929, **49**, 745). In addition dinitro-*o*-cresol was fed to rats (0·025% of diet); this resulted in considerable loss of weight but no liver damage.

Blood proteins were estimated as follows. Total protein, albumin, globulin, and non-protein nitrogen were measured in rabbits; thymol-turbidity and colloidal-gold tests (Maclagan, *Brit. J. exp. Path.*, 1944, **25**, 15 and 234) were performed in rats; the Takata-Ara test was carried out in rabbits by the method of Ucko (*J. Lab. clin. Med.*, 1942–3, **28**, 17). In addition necropsy and

detailed histological examination was carried out on all animals. The diets of all animals were carefully controlled.

The author succeeded in producing severe liver damage by the above means but he failed to find any constant or significant changes in the blood proteins. From his own results and a critical study of the literature he concludes that the liver is not the sole or main site of blood protein production, that the mechanism of such production is unknown and highly complex, and that it is possible that different fractions are formed at different sites.

C. V. Harrison

2913. **Studies in Cirrhosis of the Liver. I. Relationship between Plasma Volume, Plasma Protein Concentrations, and Total Circulating Proteins**

G. I. HILLER, E. R. HUFFMAN, and S. LEVEY. *Journal of Clinical Investigation* [*J. clin. Invest.*] **28**, 322–330, March, 1949. 1 fig., 34 refs.

The liver is not only a storage place for proteins, but the main site of formation of albumin and fibrinogen, and to a lesser extent of globulin also. When the liver is damaged both synthesis and storage are affected and a low serum-protein concentration is usual. Studies in 12 patients suffering from advanced Laënnec's cirrhosis of the liver showed that the serum-protein concentration was influenced by an associated increase in plasma volume, so that a subnormal concentration did not necessarily indicate a subnormal quantity of total circulatory protein. Plasma volumes were determined by the Gibson and Evans dye method, and diffusion of the dye into ascitic fluid was for practical purposes excluded. Total blood volume was calculated from the plasma volume and venous haematocrit values. Liver function tests—thymol turbidity, cephalin–cholesterol flocculation, hippuric-acid excretion, and bromsulphalein excretion—gave abnormal results in all the patients studied.

In the 12 patients, on whom the authors carried out 80 tests, the total circulatory protein, calculated from blood volume and protein concentration, was found to be within theoretical normal limits in 69 instances. The total circulatory globulin value was above the theoretical normal in every subject tested. The plasma volume was found to be increased—in one case up to 5,540 ml. as against a calculated normal figure of 2,750 ml.—but the degree of increase bore no relation to the presence or absence of ascites, anaemia, or oedema. Clinical improvement in several cases appeared to be related to the ability to maintain a level of total circulatory albumin above the predicted minimal value, even though the albumin concentration in the serum—often wrongly used as a guide to prognosis—was abnormally low. The raised plasma volume cannot be explained on the basis of hypoproteinaemia or of sodium retention, and the authors suggest that it may be associated with an increase in the total capacity of the vascular system due to the presence of a large liver and extensive collateral circulation in all these cases and, in two of them, of a large spleen. [No evidence in support of this suggestion is put forward.] *Thomas Hunt*

2914. **Correlation of Liver Function and Liver Structure. Clinical Applications**

H. POPPER, F. STEIGMANN, K. A. MEYER, D. D. KOZOLL, and M. FRANKLIN. *American Journal of Medicine* [*Amer. J. Med.*] **6**, 278–291, March, 1949. 6 figs., 45 refs.

The authors carried out 16 different liver function tests on patients with hepatic disease and attempted to correlate their results with the histological findings in 327 specimens obtained by liver biopsy. Significant correlation was found between diffuse liver-cell damage and many liver-function tests, particularly the cephalin–cholesterol flocculation, thymol turbidity, and bromsulphalein retention tests and the albumin–globulin ratio. There was also some correlation with raised serum bilirubin level (above 8 mg. per 100 ml.) and increased prothrombin time. Focal necrosis, fatty metamorphosis, and circumscribed lesions such as malignant metastases and abscesses showed little correlation with any liver function test. There was a significant correlation between a disturbed reconstruction of lobular pattern, as observed in cirrhosis, cephalin–cholesterol flocculation and thymol turbidity reactions, and raised erythrocyte sedimentation rate. [It is surprising that there was no apparent correlation with serum albumin–globulin ratio.] Markedly raised serum bilirubin level and abnormal albumin–globulin ratio showed significant correlation with Kupffer-cell activity.

Using their clinico-pathological classification of liver disease, the authors consider each disorder in turn and describe the histological and biochemical changes commonly observed, but they do not claim that results of liver function tests alone permit a histopathological diagnosis. Finally, 192 cases are analysed in such a way as to give a quantitative estimate of the increased accuracy in diagnosis which is possible when clinical observation is supplemented by biochemical tests and hepatic biopsy. *P. C. Reynell*

2915. **The Correlation of Hepatic Structure and Function**

L. W. KINSELL, H. A. WEISS, G. D. MICHAELS, J. S. SHAVER, and H. C. BARTON. *American Journal of Medicine* [*Amer. J. Med.*] **6**, 292–308, March, 1949. 10 figs., 28 refs.

From a "large group" of patients with liver disease studied clinically, chemically, and histologically, 9 cases are selected for detailed analysis. This group consists of 3 cases of acute infective hepatitis, 1 case of subacute hepatitis, and 5 cases of chronic hepatitis with alcoholism. The authors indicate the way histological and biochemical data are used for estimating the extent, duration, and activity of the disease; in 8 of the 9 cases the correlation between histological and biochemical findings was reasonably good. Activity is correlated histologically with phagocytic cellular infiltration and hepatocellular changes, particularly multinucleation and abnormalities in size and shape of cells; and chemically with cephalin–cholesterol flocculation and thymol turbidity reactions and serum bilirubin level. Extent and duration of disease are correlated histologically with

hepatocellular change and fibrosis, and chemically with abnormal bromsulphalein retention, diminished hepatic glycogen storage, and serum bilirubin level. It is suggested that chemical and histological tests alone can do no more than indicate in general terms the activity, extent, and duration of the disease process and do not permit precise clinico-pathological diagnosis.

P. C. Reynell

2916. **Serum Transfusion in Parenchymatous Hepatitis.** (Переливание сыворотки при паренхиматозном гепатите)
P. M. Alperin. Клиническая Медицина [*Klin. Med., Mosk.*] **27**, No. 2, 57–70, Feb., 1949. 6 figs.

The term " parenchymatous hepatitis " is used here to describe a group of acute liver dysfunctions, including infective hepatitis and toxic damage due to remote suppuration.

Twenty-six patients received a total of 136 transfusions of serum, as many as 6 transfusions being given in some cases. Transfusions of serum (whole, concentrated 2 to 3 times, or dried and reconstituted) were given, 200 to 500 ml. at a time, at intervals of 3 to 4 days. Fifteen actual cases are quoted, 9 of them very briefly indeed.

The treatment not only raises the serum protein level, but restores the albumin–globulin ratio to normal. It is not clear to what extent these results are due to a purely additive process, but such a process may account for the fall of about 20% in the haemoglobin concentration and erythrocyte count which was observed in the treated cases. In the studies on protein, 72 control patients with parenchymatous hepatitis, given no serum, were observed. Protein was estimated by refraction and nephelometry. In 11 cases galactose tolerance tests were carried out and revealed improvement with treatment. Tests of glucose tolerance and prothrombin activity also revealed improvement.

Of the 136 transfusions given, 125 caused no untoward reaction of any kind. Of the remainder, 9 caused a slight reaction, and 2 a moderate one. In this respect there appears to be no significant difference between whole serum and prepared sera.

The authors claim that the raising of plasma protein concentration materially aids the liver's recovery, although there may be a temporary phase of setback at the beginning of treatment and residual " latent changes " in the " recovered " liver. *Jeffrey Boss*

2917. **Influence of Nicotinic Acid on the Blood Sugar Level in Patients with Infective Hepatitis.** (Влияние никотиновой кислоты на уровень сахара крови больных острым паренхиматозным гепатитом)
E. M. Alesker. Клиническая Медицина [*Klin. Med., Mosk.*] **27**, No. 2, 70–76, Feb., 1949. 1 fig., 6 refs.

Twenty-two patients with acute infective hepatitis, 3 with hepatic cirrhosis, and 1 with hepatic secondary deposits from a gastric carcinoma were found to have resting blood sugar levels varying from 73 to 105 mg. per 100 ml. Injection of 100 mg. of nicotinic acid led to a fall in blood sugar level in 2½ hours by 10 to 50% of the resting value. In some cases a clinical hypoglycaemic state occurred. In all patients the tolerance to ingestion of 50 g. of glucose was increased by the simultaneous injection of 100 mg. of nicotinic acid. Even in this second group of experiments there were some patients who went into a hypoglycaemic state. In control experiments on healthy subjects (number not stated) 100 to 200 mg. of nicotinic acid did not lower the blood sugar level and only slightly increased glucose tolerance. The author recommends study of the effect of nicotinic acid on the resting blood sugar level and on glucose tolerance as a diagnostic aid.

[The tables are lucid and complete enough to enable the reader to make his own analysis.] *Jeffrey Boss*

2918. **The Value of the Nicotinic Acid Tolerance Test in the Diagnosis of Hepatic Disease.** (Sul valore del " test " di tolleranza all'acido nicotinico nella diagnosi delle epatopatie)
A. M. Pelocchino. *Acta Vitaminologica* [*Acta vitamin., Milano*] **3**, 78–85, April, 1949. 16 refs.

On 55 patients suffering from severe liver disease various liver function tests were performed and the results compared with those of the nicotinic acid tolerance test of Ellinger and Hardwick (*Brit. med. J.*, 1947, **1**, 672). A remarkable correlation was observed between the severity of the hepatic lesion and the increase in nicotinic acid tolerance, a fact which confirms findings of other observers. [The mechanism underlying the nicotinic acid tolerance test is unknown; it seems to be related to disturbed or increased protein catabolism.]

Z. A. Leitner

2919. **Carcinoma of the Liver and Infantilism.** (Cancro del fegato ed infantilismo)
V. Busacchi. *Endocrinologia e Scienza della Costituzione* [*Endocrinol. Sci. Costit.*] **19**, 123–144, 1948. 9 figs., bibliography.

A young man of 17 suffered from carcinoma of the liver and infantilism. The disease began in 1944; death ensued in 1948. The liver was enormously enlarged, and post-mortem examination confirmed the diagnosis of primary carcinoma. The height was 149·5 cm. and weight 39 kg. (normal: 168·5 cm. and 59·4 kg.). There were marked ascites, peripheral oedema, muscular atrophy, anaemia, and sexual under-development. Reduction of the ascites and repeated blood transfusions brought about temporary improvement. Histological examination of the testicles showed lack of development. The literature is reviewed in detail and the diagnosis of hepatogenic infantilism is made.

V. C. Medvei

2920. **Painless Jaundice**
W. F. MacFee. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **141**, 171–175, Sept. 17, 1949. 17 refs.

See also Sections Pathology, Abstract 2770; Endocrine Disorders, Abstract 2921.

Endocrine Disorders

2921. **A Case of Acute Yellow Atrophy of the Liver during Treatment of Thyroid Hyperfunction with Methylthiouracil.** (Przypadek ostrego zołtego zaniku wątroby w przebiegu ieczenia nadczynności tarczycy metylotiouracylem)
A. HORST. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] 4, 463–466, April 11, 1949. 13 refs.

Although the aetiology of acute liver atrophy is not sufficiently understood to warrant any general conclusions, it seems reasonable to suggest that thiouracil derivatives are capable of damaging the parenchyma of the liver. In the case described methylthiouracil is not thought to have been the sole causal agent but was probably one of several co-existing factors. The author concludes that during the treatment of hyperthyroidism with thiouracil derivatives considerable attention should be directed not only towards the state of the haematopoietic system but also to the possibility of liver damage.

J. H. Czekalowski

2922. **Thiouracil in Thyrotoxicosis**
D. VÉREL. *British Medical Journal* [*Brit. med. J.*] 1, 892–895, May 21, 1949. 6 refs.

A series of 62 patients with thyrotoxicosis were treated with thiouracil or methylthiouracil for periods ranging from 6 months to 4½ years. The series included all cases of the disease admitted to hospital under the care of the Aberdeen University Department of Medicine, except for a few so mild as to require phenobarbitone only for control. There were 10 males and 52 females, their ages ranging from 16 to 66 years. The most satisfactory initial dose was found to be 0·4 g. daily of thiouracil and 0·2 g. daily of methylthiouracil, the usual maintenance dose being 0·2 g. daily of thiouracil and 0·1 g. daily of methylthiouracil; methylthiouracil was used as a routine in all the later cases.

Of the 62 patients treated one died of suppurative bronchiectasis and 2 underwent thyroidectomy, because of persistent granulopenia in one case and great thyroid enlargement in the other. In all the remaining 59 patients the disease was effectively controlled by the drug and the majority were at full work within 6 weeks. Of 13 patients under observation for 3 years or more, 5 had remained free from relapse after 33 to 39 months without thiouracil, 3 had remained well after 21 to 33 months without the drug, 3 had relapsed after stopping treatment but had been brought under control again with further thiouracil, and 2 had only stopped taking the drug within the past 6 months. Pregnancy had occurred in 3 patients: in 2, thiouracil was stopped during the latter part of pregnancy and a normal child was born in each case; in the third, thiouracil was continued throughout the pregnancy and the infant was born with an easily palpable thyroid which, however, had become impalpable after one month, the child being otherwise normal. Granulopenia occurred in 8 cases' but in only one was there an associated infection: in the other 7 it was discovered on routine examination and the thiouracil was stopped; the leucocyte count then rose rapidly, no penicillin being given, and 4 of these patients later resumed taking thiouracil without developing further granulopenia. Myxoedema occurred in one patient 19 months after thiouracil was stopped, and temporary diplopia occurred in 2. Auricular fibrillation was present before treatment in 10 patients: in 4 it was continuous and in one of these sinus rhythm was restored by thiouracil alone; in 5 it was paroxysmal and in 4 of these it was controlled by thiouracil alone. Koilonychia was seen in 7 patients, only one of whom had a severe degree of anaemia: the nails became normal in 4 cases during thiouracil treatment, no iron being given, and no rise in haemoglobin level having occurred in 3 of them.

A. R. Kelsall

2923. **Influence of Vitamin A on the Histology of Some Endocrine Glands in Different Phases of Thyroid Activity.** (Influenza della vitamina A sul quadro istologico di alcune ghiandole endocrine in diversi stadi di funzionalita tiroidea)
L. BASCHIERI and F. FERRI. *Acta Vitaminologica* [*Acta vitamin., Milano*] 3, 69–77, April, 1949. 16 figs., 36 refs.

Administration of vitamin A, 10,000 units subcutaneously on alternate days, did not modify substantially the histological appearance of the thyroid or the pituitary of guinea-pigs given 0·1 mg. of thyroxine every third day for 30 days, although it exerted an action antagonistic to thyroxine and increased the effect of methylthiouracil. The adrenal cortex and testes of these animals, however, showed very definite changes after administration of thyroxine, methylthiouracil, and vitamin A, the abnormalities produced by the first two when given alone being replaced by the appearance of normal activity. The authors suggest that the antagonistic action of vitamin A to thyroxine might be due to its capacity to increase the production of the steroid hormones. *Z. A. Leitner*

2924. **Separation of Central and Peripheral Metabolic Stimulatory Effects; Effect of Thyroxine.** [In English]
B. ISSEKUTZ, G. HETÉNYI, and I. FEUER. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] 78, 512–520, April, 1949. 1 fig., 14 refs.

The *in vitro* oxygen consumption of duck erythrocytes is not significantly altered either by cooling the duck or by injecting amphetamine, procedures which increase the metabolic rate of the whole bird by a central mechanism. However, after administration of 2 : 4-dinitrophenol, which increases the duck's metabolic rate by a peripheral action, the respiration of erythrocytes is significantly

increased. Adrenaline, also acting peripherally, has the same effect on the erythrocytes, although the duck's metabolic rate is reduced because of the circulatory effects of the adrenaline. Increase in respiration of erythrocytes gives a satisfactory indication that a drug which stimulates metabolism is acting peripherally. Nine ducks given daily subcutaneous injections of 0·5 to 1·0 mg. of thyroxine per kg. for 5 days had an increased metabolic rate, and the *in vitro* respiration of their erythrocytes was significantly raised. The plasma of the thyroxine-treated ducks did not increase the oxygen consumption of normal erythrocytes; the thyroxine is only effective when it has been fixed by the cells.

Derek R. Wood

2925. **Influence of Steroid Hormones on Granulation Tissue**

M. TAUBENHAUS and G. D. AMROMIN. *Endocrinology* [*Endocrinology*] **44**, 359–367, April, 1949. 5 figs., 17 refs.

The author studied the granulation tissue in the walls of abscesses formed by injecting turpentine subcutaneously in rats. Rats into which desoxycorticosterone (1 mg. daily for 5 weeks) had been injected showed a greater fibroblastic response, thicker granulation tissue, and more collagen deposition than control rats, and cicatrization was completed earlier. Rats injected for the same period with oestradiol dipropionate (1 mg. daily) or testosterone propionate (2·5 mg. daily) before turpentine injection showed a subnormal granulation response: the abscesses were poorly defined, with thin walls almost devoid of granulation tissue and with scanty fibroblasts and collagen; the inhibition produced by oestrogen was more marked than with androgen. In rats which had been both castrated and subjected to adrenalectomy the granulation response was only slightly less than in intact rats.

Peter C. Williams

2926. **Insulin Hypersensitivity Following the Administration of Desoxycorticosterone Acetate**

C. P. CHENG and G. SAYERS. *Endocrinology* [*Endocrinology*] **44**, 400–408, May, 1949. 2 figs., 17 refs.

The authors report a series of experiments on rats which, after the implantation of tablets of desoxycorticosterone acetate, were found to be unusually sensitive to insulin, doses which had produced only a moderate fall in blood sugar level in normal rats causing hypoglycaemic coma and death. The increase in sensitivity was nearly as great as that produced by adrenalectomy. The increased sensitivity was overcome by the injection of adrenal cortical extract together with the insulin. All the tests were carried out on rats with no adrenal medulla, so that adrenaline secretion was not involved. These results imply that the administration of desoxycorticosterone in some way interferes with the secretion of those 11-oxygenated corticosteroids which influence carbohydrate metabolism. Consideration of the relevant literature leads the authors to prefer an indirect suppression of adrenal cortical secretion as the explanation rather than a direct influence on the adrenals. In their view the administered desoxycorticosterone suppresses the secretion of adrenocorticotrophin by the pituitary, and the secretion of the 11-oxygenated corticosteroids is diminished as a result.

[If the desoxycorticosterone suppresses total adrenal cortical function, whether directly or indirectly, then the secondary dangers of overdosage must be considered in the clinical use of this steroid.] *Peter C. Williams*

2927. **Addison's Disease: A Clinical Review of Thirty-four Cases, with Reports of Three Cases Showing Associated Thyrotoxicosis**

J. C. HOUSTON and T. M. L. PRICE. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **97**, 254–267, 1948. 5 figs., 25 refs.

2928. **Carcinoma of the Parathyroid Gland with Hyperparathyroidism**

O. L. V. DE WESSELOW and H. E. DE WARDENER. *Lancet* [*Lancet*] **1**, 820–823, May 14, 1949. 3 figs., 9 refs.

The authors refer to 3 cases, recorded in the literature, of parathyroid hyperfunction with evidence of clinical and histological malignancy and give clinical details of one further case.

The patient in their case was a woman of 35 who was first admitted to hospital in 1942 with classical signs and symptoms of hyperparathyroidism. A parathyroid tumour was removed on no fewer than 5 separate occasions between this date and 1948, and two courses of *x*-ray therapy were given. Symptomatic relief and lowering of the serum calcium level followed these procedures. In most of the relapses there was a sudden onset of symptoms and an associated cardiac failure, due probably to the high serum calcium level. Histological section of the tumour removed at the fifth operation showed a low degree of malignancy. *Geoffrey McComas*

2929. **Changes in the Parathyroids in Renal Insufficiency.** (Изменения околощитовидных желез при почечной недостаточности)

M. A. TISHCHENKO. Архив Патологии [*Arkh. Patol.*] **11**, No. 2, 43–49, March–April, 1949. 2 figs., 17 refs.

Parathyroids were studied in 18 subjects dying of renal disease. The average combined weight of the glands was 272 mg., compared with 110 mg. in the controls. Microscopically, the main features were the relative or complete absence of fat, and predominance of the light chief cells. Oxyphil cells were few in number, and there were a few scattered foci of colloid. The pathogenesis of this hyperplasia is discussed, and the author suggests that it is compensatory in nature in cases of disturbance of calcium and phosphate blood levels.

L. Crome

2930. **Primary Hyperplasia of the Parathyroid Glands Associated with Ulcers in the Oesophagus and Duodenum and Polycythemia of the Splenomegalic Type.** [In English]

F. BERLIN. *Acta Medica Scandinavica* [*Acta med. scand.*] **135**, 18–24, 1949. 15 refs.

2931. **The Effect of Adrenocorticotrophic Hormone in Congenital Adrenal Hyperplasia with Virilism and in Cushing's Syndrome Treated with Methyl Testosterone**
R. A. LEWIS and L. WILKINS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **28**, 394–400, March, 1949. 11 refs.

In this study, the effects of injection of a single large dose of adrenocorticotrophic hormone were observed in 3 young patients. Two were girls, aged 6½ years, with congenital adrenal hyperplasia and so-called female pseudohermaphroditism (female genital hermaphroditism), and the other was a boy of 16½ years with Cushing's syndrome who had received treatment by pituitary irradiation (20 doses of 95 r) and subsequently with methyl testosterone, 30 mg. daily for some 3 years, up to and including the time of the reported investigation. The patients were kept on a constant diet, no observations being made during the first 3 days; the next 3 days served as a control period, treatment being given during the following 24 hours. Observation continued for a further 24-hour carry-over period, followed by a 3-day post-treatment control period.

The results in the case of the boy with Cushing's disease can be summarized by the statement that they resembled those reported by other authors for normal individuals. Since there had been considerable treatment (which was continued during the investigation) and the disease was quite stationary (though whether this was because of treatment or because of spontaneous remission could not be decided) these findings are not remarkable. In contrast, the response of the 2 girls with virilizing adrenocortical hyperplasia showed the unusual feature of *increased* sodium excretion, marked in one case (138 milliequivalents (m.eq.) a day in the control period, 468 m.eq. on the day of treatment, and 81 m.eq. a day on the following 4 days) and moderate in the other. In the boy with Cushing's syndrome, the sodium excretion fell from 142 m.eq. per day to 39 m.eq. on the day of treatment, remained at 38 m.eq. on the following day, and then rose to 133 m.eq. per day for the next 3 days. With the increased sodium excretion there was also an increase in chloride excretion and in the case of the girl with marked sodium and chloride diuresis there was a slight fall in serum sodium and chloride levels.

The authors believe that the above findings represent the first clear-cut example of production by a trophic hormone of qualitatively different effects upon the same endocrine gland and suggest that the secretory activity of the adrenal in cases of congenital adrenal hyperplasia with virilism differs qualitatively from that in other conditions. *G. I. M. Swyer*

2932. **Gynaecomastia During Treatment with Amphetamine**
P. H. TOOLEY and C. LACK. *Lancet* [*Lancet*] **1**, 650–651, April 16, 1949. 1 fig., 7 refs.

The authors noticed swelling of the breasts in several male subjects receiving amphetamine sulphate. The swelling was sometimes asymmetrical and usually slightly tender. Five illustrative cases are reported briefly. The total dosage of the drug before the development of this sign was 175 and 170 mg. in 2 boys of 17 and 15 years respectively, and 4,480 mg. in a man of 38. [The total dosage is not recorded for the other 2 patients, in one of whom (a psychopath) impotence also developed.] In one girl of 9 years uterine bleeding occurred after she had received 2,200 mg. of the drug in 98 days, and persisted until the amphetamine was stopped after a month. Subsequent batches of amphetamine did not produce gynaecomastia, even in subjects known to be susceptible, but the active batch reproduced similar signs in hypophysectomized rats. The authors conclude that the effects were due to an impurity of considerable oestrogenic potency in the amphetamine sulphate; substances closely related in structure to the oestrogens are formed during one of the chemical processes in the preparation of amphetamine sulphate. *A. R. Kelsall*

2933 (*a*). **A New Procedure for the Determination of the Antidiuretic Principle in the Urine**
A. GROLLMAN and B. WOODS. *Endocrinology* [*Endocrinology*] **44**, 409–414, May, 1949. 16 refs.

2933 (*b*). **The Antidiuretic Hormone in the Urine in Experimental and Clinical Hypertension**
M. E. ELLIS and A. GROLLMAN. *Endocrinology* [*Endocrinology*] **44**, 415–419, May, 1949. 12 refs.

The available methods for the estimation of the antidiuretic principle in the urine, involving concentration by dialysis, are unreliable since there is evidence that the membranes used are not entirely impermeable to the hormone, which may therefore be partially lost. In the first of these two papers a much more efficient method of extraction is described in which adsorption on charcoal is used in place of dialysis. Application of this method to commercial posterior pituitary extract resulted in good recovery of the antidiuretic principle, and it was also shown that oxidation of the extract with hydrogen peroxide will deprive it of its capacity to increase chloride excretion (chloruretic activity) without affecting its antidiuretic activity.

With the improved extraction method it was possible to demonstrate antidiuretic activity in the urine of normal dogs and human beings. Much greater amounts are excreted in the urine of patients with hypertensive cardiovascular disease and of dogs and rats with hypertension due to renal ischaemia. Chloruretic activity, however, was not demonstrable in the urine of hypertensive or of normal subjects. These results are similar to those previously reported by other workers showing an increased excretion of antidiuretic factor in patients with other conditions involving salt and water retention (cirrhosis of the liver with ascites, acute glomerular nephritis, and eclampsia). Since the chloruretic activity may equally well be destroyed by oxidation *in vivo* and *in vitro*, its absence in such cases need not be considered an overruling objection to regarding the antidiuretic principle as originating in the posterior pituitary. The authors do not think that increased posterior pituitary activity has any causative significance in these conditions, but that it is more probably a secondary effect of altered salt and water metabolism due to disordered function of the liver or kidney. *Peter C. Williams*

Dermatology

2934. **Grenz Ray (Supersoft Roentgen Ray) Therapy of Cutaneous Diseases**
S. L. HANFLING. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **58**, 390–397, Oct., 1948. 12 refs.

The results in 3 groups of patients with various dermatoses treated with grenz rays are presented and compared with those obtained with conventional superficial *x*-irradiation. It is suggested that grenz-ray treatment compares favourably with *x*-ray treatment for diseases of the skin, and that the use of grenz rays with a half-value layer of 0·028 mm. or less of aluminium appears to be a safe form of physical therapy. Cases of special interest are described and the results in 58 patients (76 series of irradiations) are analysed in four detailed tables. *G. B. Mitchell-Heggs*

2935. **Present-day Tendencies in American Dermatology.** (Tendances actuelles de la dermatologie aux États-Unis)
J. L. CHAPUIS. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **9**, 158–167, March–April, 1949.

Observations are made on a 6 months' visit to some of the important dermatological teaching centres in the U.S.A. The author notes the tendency for pathological investigations to take precedence over careful clinical examination. Radiotherapy is much more widely used than in France; some authorities are pressing for a more precise statement of the indications for radiotherapy and for better instruction of practitioners in the practical details of its application. The use of topical applications is less common than in France, the medicaments are different, and many well-known French remedies and formulae are unknown. Sulphonamides are seldom used as local applications because of their liability to cause sensitization. Penicillin is not abused as a local application; tyrothricin, although sometimes an irritant, is recognized as an efficacious remedy. Dietary regimens are ordered for very many of the patients suffering from dermatoses.

The American student has not the same advantage in seeing large numbers of patients and following their progress as the student at the St. Louis Hospital in Paris, where there are large numbers of in-patients and out-patients. Clinical instruction takes second place to lectures and seminars. Postgraduate instruction for intending specialists is confined to dermatology and there is not the contact with general medicine which exists in France.

A summary of the latest advances in treatment of syphilis is given. The author finds in the U.S.A. no tradition such as that associated with the great names in French dermatology; the main influences are German and Austrian. *James Marshall*

2936. **The Clinical Reaction of the Skin to Mustard Gas Vapour**
D. C. SINCLAIR. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm. Syph.*] **61**, 113–125, April, 1949. 3 figs., 16 refs.

Men undergoing military training in the desert were investigated for the effects of burns from mustard-gas vapour. In a series of 143 men 95 showed severe reaction, including oedema and vesication, but the remainder suffered only a slight erythema. Certain sites were more vulnerable than others, the neck and scrotum being most commonly affected. These were not necessarily the most severely burned sites, reactions generally being most marked about the axillae and penis.

It is suggested that there is nothing specific about the reaction, which is the response of the skin to a slowly acting irritant. The long latent period before the development of erythema is comparable with that observed in ultraviolet-light burns. *John T. Ingram*

2937. **Podophyllotoxin**
M. SULLIVAN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **60**, 1–13, July, 1949. 31 refs.

2938. **Treatment of Eczema with Unsaturated Fatty Acids.** (Le traitement de l'eczéma par les acides gras non saturés)
E. AZERAD and C. GRUPPER. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **25**, 684–689, Feb. 28, 1949. 15 refs.

Eczema, especially infantile eczema, was treated by giving unsaturated fatty acids by mouth. At first fresh lard was used. Infants and children up to the age of 2 were given 30 to 60 g. daily; adults took 100 g. daily. Satisfactory improvement was obtained but cure was uncommon; the addition of vitamin B_6 made no difference. Failures were due to the variability of the linoleic acid content of the lard and to the difficulty of continued administration of such large quantities to some of the infants. Encouraging results with wheat-germ oil were due to the presence of linoleic acid in the oil. Synthetic vitamin E had no effect on eczema. Finally, purified linoleic acid and its ethyl ester were used. Infants were given 100 to 200 drops daily, and adults 300 to 400 drops daily. There were no digestive upsets. The acid was flavoured with mint, aniseed, or cinnamon; the ethyl ester was more pleasant to take. The only local application was a 10% tar ointment or paste. Of the first hundred patients treated with unsaturated fatty acids, 58 were infants, 18 were children, and 24 were adults. In 52 the rash disappeared completely, in 31 pruritus and weeping ceased, and in 17 results were unsatisfactory. All the failures were in adults.
E. Lipman Cohen

2939. **Estrogenic Ointments. Cutaneous Effects of Topical Applications of Natural Estrogens, with Report of Three Hundred and Twenty-one Biopsies**
J. J. ELLER and W. D. ELLER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **59**, 449–464, April, 1949. 5 figs.

Ointments containing varying concentrations of oestrogens were applied continuously or by daily inunction to a 10×10 cm. area of the skin of men, young women, post-menopausal women, and old men. The effects were estimated by biopsy at 10-day intervals, skin from the treated area being compared with skin from the corresponding area on the opposite side, which was treated with the ointment base alone. There were no significant changes in the control skin or in the treated skin of men or young women. In the skin of post-menopausal women the atrophic changes of senility gave place to normal regeneration of epithelium and some slight regeneration of collagen and elastic tissue, but no evidence of abnormal mitosis or neoplastic change. The changes were proportional to the concentration of oestrogen and to the duration of contact. The changes reached a maximum within 30 to 50 days. The amount of oestrogen absorbed from these applications must have been very small but they did effect some little change in the character of vaginal smears in some cases.
John T. Ingram

2940. **Role of Spectacle Lenses in Production of Cutaneous Changes, Especially Epithelioma**
E. F. CORSON, G. M. KNOLL, H. A. LUSCOMBE, and H. B. DECKER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **59**, 435–448, April, 1949. 3 figs., 3 refs.

Carcinomata and chronic inflammatory changes in the skin of the cheek are reported in 12 patients, in whom the site involved was where refracted light conducted from the upper to the lower edge of rimless spectacle lenses worn by the patient came to a focus on the skin. Experimentally it was shown that temperature changes were produced at these sites on exposure to sunlight or strong electric light—a "burning glass" effect—and it is suggested that repeated injury from this source was responsible for the skin changes. The use of "rim black" on the upper and lower edges of the lenses or spectacle frames protects against such damage.
John T. Ingram

2941. **Clinical Experiences with "Antistin" in some Skin Diseases.** (Kliniczne doświadczenia z antystyną w niektórych chorobach skóry)
K. BOCZAR. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **4**, 356–361, March 21, 1949. 31 refs.

The favourable response of various allergic skin conditions to antihistamine drugs was confirmed in a group of 25 patients. "Antistin" in a dose of 100 mg. was given thrice daily in tablet form but the intravenous or intramuscular route was used in cases which failed to respond after 7 days of oral administration. The cases consisted of acute eczema, urticaria, erythema solare, localized pruritus, and erythema multiforme. In 20 cases recovery was obtained after 3 to 14 days of treatment. The cases which failed to improve were those of senile pruritus and of subacute eczema in children. In erythema multiforme the results were surprisingly good and in most cases there was a marked relief and diminution of pruritus. A few patients complained of headaches and somnolence but no severe toxic signs were met with.
J. T. Leyberg

See also Section Hygiene and Public Health, Abstracts 2660–1.

2942. **Investigations on the Development of Microbic Growth in the Axillary Region during the First Weeks of Extrauterine Life.** (Recherches sur l'ensemencement microbien de la région axillaire pendant les premières semaines de la vie extra-utérine)
A. DELMOTTE. *Archives Belges de Dermatologie et de Syphiligraphie* [*Arch. belges Derm. Syph.*] **5**, 1–29, April, 1949.

This careful bacteriological study confirmed the theoretical views of Jadassohn that the skin of the foetus is sterile; at the time of birth, a certain number of organisms from the maternal genital tract are deposited on the skin and in the natural cavities of the child. Only a limited number of the organisms normally present in the maternal genital tract will adapt themselves to the conditions of existence on or in the infant to become true saprophytes.
James Marshall

2943. **Transverse Net in the Diagnosis of Onychomycosis**
J. ALKIEWICZ. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **58**, 385–389, Oct., 1948. 5 figs., 3 refs.

A pathognomonic sign of onychomycosis, the transverse white net, is described. This phenomenon is visible in the majority of cases of fungus infection of the nail but only with a lens and through an oil drop. The visible white lines of the net correspond to air-filled tunnels in the nail plate. Photomicrographs of a case are reproduced which demonstrate the appearances.
G. B. Mitchell-Heggs

2944. **Ringworm of the Scalp. Treatment by *X*-ray Epilation Without Subsequent Local Application**
F. L. LYDON, T. STEPHANIDES, and T. M. ROBB. *British Medical Journal* [*Brit. med. J.*] **1**, 523–524, March 26, 1949. 3 refs.

The authors regard local treatment with fungicides as unnecessary in combination with *x*-ray epilation They advise their patients simply to wash the scalp with soap and water from the fifteenth day after treatment until epilation is complete, and to apply ung. adipis lanae to soften scales. They review 103 cases of tinea capitis treated solely by *x*-ray epilation and claim that all were cured. Although *x* rays are not parasiticidal, they may either reduce the vitality of the fungus or bring about a

tissue change which lessens the chance of contamination of the new hair. Thus, with a satisfactory epilation it may not be necessary to keep children away from school for more than 6 weeks. *E. W. Prosser Thomas*

2945. **Vioform in the Treatment of Skin Diseases**
I. MARTIN-SCOTT. *British Medical Journal* [*Brit. med. J.*] **1**, 837–840, May 14, 1949. 11 refs.

Quinoline derivatives have been used in dermatology for a number of years. " Vioform " is 5-chloro-7-iodo-8-hydroxyquinoline and is used internally in the treatment of amoebiasis. The author used 3% vioform cream in a water-soluble base and a 3% ointment in a petroleum jelly base in the treatment of a variety of dermatoses in 115 patients. Results were remarkably good in sycosis barbae, post-auricular dermatitis, and other pyococcal dermatoses. Acne was not relieved. The preparations were found to be relatively non-irritant and sensitization did not readily occur. The antipruritic affect was not marked except in infected eczematous cases. *John T. Ingram*

2946. **The Topical Use of Vioform in Dermatology**
J. OVERTON. *British Medical Journal* [*Brit. med. J.*] **1**, 840–842, May 14, 1949. 27 refs.

The indiscriminate use of chemotherapeutic and antibiotic agents in the treatment of skin diseases may lead to drug sensitization and the development of resistant strains of organisms. In a search for a drug to replace the sulphonamides and penicillin in external applications, the author found " vioform " (5-chloro-7-iodo-8-hydroxyquinoline) to be a safe and non-irritant antiseptic, effective in pyogenic dermatoses especially of the chronic type. Its antiseptic action is not due to the liberation of iodine.

A 3% vioform cream and an ointment were used in the treatment of 176 patients—control preparations of the same colour being used to assess results. Sycosis barbae, seborrhoeic dermatitis, otitis externa, and impetigo responded well. Itching was relieved in cases of eczema. There was a low incidence (4·5%) of intolerance.
John T. Ingram

2947. **The Use of Nicotinamide in Tuberculous Affections of the Skin.** (L'esperienza ad oggi sopra l'uso dell'amide nicotinica in affezioni tubercolari della cute)
U. SILVESTRI. *Acta Vitaminologica* [*Acta vitamin., Milano*] **3**, 59–66, April, 1949. 15 figs., 7 refs.

Administration of 2 g. of nicotinamide daily by mouth or on alternate days intravenously, no other treatment being given, brought about clinical healing in cases of lupus vulgaris. [The number of patients treated and the percentage cure are not specified.] The duration of treatment (2 to 8 months) depended on the age, vascularization and scarring of the lesion, and intravenous administration of nicotinamide usually shortened the time necessary for treatment. At the same time regression of concomitant tuberculous manifestations in other organs could be observed. Apart from flushing no toxic effects were noticed. Experiments are described which are claimed to have demonstrated an inhibitory influence of nicotinamide on tubercle bacilli *in vitro*.
Z. A. Leitner

2948 (*a*). **Kaposi's Varicelliform Dermatosis: A Virus Pyodermia**
T. ANDERSON. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm. Syph.*] **61**, 157–166, May, 1949. 5 figs., 18 refs.

2948 (*b*). **A Case of Kaposi's Varicelliform Eruption (Systemic Herpes Simplex) with Dendritic Ulceration of the Cornea**
R. VARLEY and T. KLETZ. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm. Syph.*] **61**, 166–170, May, 1949. 18 refs.

2948 (*c*). **A Fatal Case of Kaposi's Varicelliform Eruption**
J. C. S. LEVERTON and F. A. WHITLOCK. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm. Syph.*] **61**, 170–173, May, 1949. 2 figs., 2 refs.

[These are three good reports, in fortunate juxtaposition, of what appears to be a recognizable clinical picture, if some liberties with Kaposi's original description allow the use of his name in the title.] Seven cases of varicelliform eruption are described in considerable detail with good photographs. Three of the cases in Anderson's paper were shown to be " due to infection by vaccinia virus ". In the other 2, another virus (possibly that of herpes simplex) may have been involved and the term " virus pyodermia " is suggested as " a more accurate designation ". The case described by Varley and Kletz may have been due to the herpes simplex virus, the two localizations suggesting a " different phase of sensitization to the virus ". Leverton and Whitlock state that in their case, " a virus infection affecting the upper respiratory tract and conjunctivae had been present in the child's family, but it is improbable that the virus was that of herpes simplex, and it certainly was not vaccinia ".

The presence of some upper respiratory infection, called " influenza " usually by the sufferers, was noted in Anderson's cases. It would seem that a single causative agent for Kaposi's varicelliform eruption is far from established and that in Anderson's words " it is desirable that such cases should be more closely studied in respect of virus aetiology ". *J. E. M. Wigley*

2949. **Radiotherapy of Recurrent Herpes.** (Nouvelles données sur la radiothérapie de l'herpès récidivant)
J. FRANKL. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **9**, 168–170, March–April, 1949. 4 refs.

Excellent results are reported in recurrent herpes febrilis from the use of soft *x* rays in the inflammatory stage. One or two doses sufficed in the 12 cases reported. The affected area and the skin for a fingerbreadth around are treated; the dosage is 130 r at 80 kV and 3 mA with a 1·2 mm. Al. filter, at a distance of 23 cm.
James Marshall

2950. **Gold Stomatitis. Acute Ulcerative Buccal Lichen Planus Treated by BAL.** (Stomatite aurique. Lichen plan aigu ulcéreux buccal biotropique traité par le B.A.L.)
—. MORDANT. *Archives Belges de Dermatologie et de Syphiligraphie* [*Arch. belges Derm. Syph.*] **5**, 63–66, April, 1949. 10 refs.

The author reports a rapid cure when BAL was used in the treatment of a case of lichen-planus-like stomatitis occurring during the treatment of polyarthritis with gold.
James Marshall

2951. **Hereditary Ectodermal Dysplasia.** (Dysplasie ectodermique héréditaire)
A. TANISSA. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **9**, 171–175, March–April, 1949. 23 refs.

The classic triad in this condition is anhidrosis, hypotrichosis, and anodontia. To this the author would add cranio-facial dysplasia. The nose is always deformed, sometimes saddle-shaped and sometimes negroid, and obliquity of the eyes gives to the patient a mongolian appearance. This description is the same as that of the " ozaena facies " and, indeed, atrophic rhinitis is usually also present. Dyschromias may also be found, for example, hyperpigmented plaques, leukoderma, and vitiligoid patches. Evidence of hypofunction of the adrenal and pituitary glands can also be demonstrated.
James Marshall

2952. **Haemangiectasia Hypertrophicans of Parkes Weber.** (Sobre la haemangectasia hypertrophicans de Parkes Weber)
A. V. FERRARI. *Actas Dermo-sifiliográficas* [*Actas Dermo-sif.*] **40**, 577–596, March, 1949. 4 figs., 46 refs.

In this paper the literature is reviewed, and the author describes the symptomatology of the condition and 3 cases in which both legs, the face, and the left leg respectively were affected. The classic triad consists of vascular naevi, varices, and hypertrophy of a part of the body. Associated lesions include eczema, varicose ulcers, ichthyosiform lesions, alopecia, sensory changes, and hyperhidrosis.
James Marshall

2953. **The Direct Effect of Steroids on the Senile Human Skin. A Preliminary Report**
J. W. GOLDZIEHER. *Journal of Gerontology* [*J. Gerontol.*] **4**, 104–112, April, 1949. 5 figs., 8 refs.

It has been shown by the author that the application of steroids in high concentration to the senile skin results in regeneration of the epidermis. The steroids examined particularly were androgens and oestrogens. A solution of testosterone propionate in ether (1 mg. per ml.) and a solution of oestrogen (chiefly oestrone) in alcohol-ether (0·5 mg. per ml.) were used. The selected reagent was sprayed with a syringe in 1 ml. doses on to a marked area of thigh skin, 5×5 cm., twice daily for a period of 23 to 42 days and biopsy carried out every 5 days. It was found in 6 elderly subjects, 5 male and 1 female, that the effects of androgen and oestrogen on the skin histology were identical and independent of the patient's sex. Definite changes were seen in the epidermis within 5 days of starting treatment with androgen, and 10 days with oestrogen, the main changes being an increase in size of the rete pegs and a thickening of the epidermis. There was also increased pigmentation of the basal layer. This preliminary report is intended to stimulate further investigation on the ageing skin.
H. R. Vickers

See also Section Radiology, Abstract 2756.

2954. **Observations on the Structure and Formation of Bullae. II.**
G. H. PERCIVAL and P. W. HANNAY. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm. Syph.*] **61**, 77–89, March, 1949. 23 refs.

In dealing with the bullae of dermatitis herpetiformis, pemphigus, and erythema multiforme the authors describe in detail the experiments and methods used to determine (1) the response of the cutaneous vessels in the immediate vicinity of the bullae to histamine; (2) the permeability of the tissues involved to congo red, methyl violet, sulphathiazole, and plasma proteins; (3) the hydrostatic pressure of the fluid contained in the bullae and the method of its production; and (4) the chemistry of the fluid. The results obtained and the mechanisms involved are discussed.
G. B. Mitchell-Heggs

2955. **Porphyric Bullous Dermatosis**
I. ZELIGMAN and M. BAUM. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **58**, 357–371, Oct., 1948. 3 figs., 15 refs.

The bullous eruptions which occur in porphyria are reviewed, with special emphasis on the importance of trauma as a causative factor. The case is reported in detail of an alcoholic patient with chronic porphyria in whom bullae appeared following trauma on those parts of the skin normally exposed to sunlight. The authors suggest that the bullous eruptions present in porphyric patients, whether hitherto named hydroa aestivale or epidermolysis bullosa, are essentially the same and are the result of the presence of photodynamic uroporphyrin in the skin which makes it more susceptible to light, to trauma, or both combined. They propose the use of the term " porphyric bullous dermatosis " in such cases.
G. B. Mitchell-Heggs

2956. **Reflections on the Senear–Usher Syndrome.** (Réflexions à propos de la pemphigoïde séborrhéique)
E. GRIVEAUD and J. ACHARD. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **9**, 129–148, March–April, 1949. 6 figs.

The clinical course and histological findings are described in 12 cases of the Senear–Usher syndrome. In only 2 cases did the facial eruption resemble that of lupus erythematosus; in all the others there was a rash of seborrhoeic dermatitis type. Treatment is discussed, but no new suggestions are made. [This article is well illustrated and gives an excellent account of the condition.]
James Marshall

Venereal Diseases

2957. **Histogenesis and Parasitology of Lymphogranuloma Venereum.** (Histogenèse et parasitologie du ganglion poradénique)
M. FAVRE. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **9**, 249–275, May–June, 1949. 19 figs., 1 ref.

A careful and complete study was made of the histological appearances and development of the lymph-node lesions in lymphogranuloma venereum. " The characteristic lesions develop in the lymph nodes or peri-nodal tissues as little collections of polynuclear leucocytes and free connective-tissue cells. The micro-abscess grows slowly and around it the inflamed connective tissue gradually builds up a continuous barrier or girdle of so-called epithelioid cells. Degeneration of the cellular elements, already visible in the earliest stages of the micro-abscess, is now more evident and the process stops only when all the elements of the abscess are transformed into a homogeneous mass in which no nuclei are to be seen. All stages of transition can be seen, from the micro-abscess to the large enclosed collection which later becomes the colliquative gumma." [The descriptions are well illustrated with photomicrographs and drawings, and the article is well worth reading in the original.]

James Marshall

2958. **Aureomycin Treatment of Acute Gonorrhea in Males**
H. S. COLLINS, H. TROUSDALE, T. F. KAISER, F. C. REGAN, and M. FINLAND. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **33**, 263–269, May, 1949. 9 refs.

Aureomycin has proved highly effective against gonococci *in vitro* and sensitivity tests have shown it to be superior to streptomycin, bacitracin, polymyxin D and B, and sulphadiazine. Against the same strains of gonococci, however, penicillin was more active than aureomycin. The latter given by mouth in total doses of 1·0 to 3·5 g. over a period of 12 to 36 hours cured 87% of 122 cases of acute gonorrhoea in males; some cases classified as failures were possibly cases of re-infection. This early experience suggests that the best results are achieved with 2·5 g. given over a period of not less than 36 hours. The clinical response in successful cases was prompt, and in one case an acute epididymitis settled down rapidly. No toxic effects were noted in this series.

The authors conclude that aureomycin is a second choice to penicillin in the treatment of gonorrhoea but feel that it may be particularly useful in cases of mixed infection or for in-patients sensitive to penicillin. [Recent work indicates its value in non-specific urethritis, especially in those cases in which pleuropneumonia-like organisms are present.]

S. M. Laird

2959. **Examination of Living Gonococci by Phase Contrast.** (Über die Untersuchung lebender Gonokokken mit dem Phasenkontrastverfahren)
H. HASELMANN and W. KAPPEL. *Archiv für Dermatologie und Syphilis* [*Arch. Derm. Syph., Wien*] **187**, 501–505, 1949. 2 figs., 20 refs.

Phase-contrast examination of living gonococcal cultures on a thin agar medium is described. The individual cocci are about twice as large as those obtained with the customary stained specimen. Also the usual arrangement of diplococci is often missing. With unfavourable growth conditions certain degenerative changes are described. The process of division can be easily observed and takes about 15 minutes. It occurs always in pairs which show changes in shape, protoplasmic movements, and finally division.

G. W. Csonka

2960. **Morphology, Cultural Characteristics, and a Method for Mass Cultivation by the Reiter Spirochete**
A. GELPERIN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **33**, 101–113, March, 1949. 5 figs., 19 refs.

In order to study the antigenic components of spirochaetes it is necessary to cultivate them on a large scale. For this purpose the Reiter strain was chosen; this organism can easily be distinguished from *Treponema pallidum* since it is one and a half times to three times as thick, two to four times as long, and has coarse spirals and sluggish movements. This form is seen when the organism is subcultured every 5 to 7 days in a medium containing agar, but when the organism is incubated for 2 to 3 weeks various forms are seen, such as transparent spheres at the end of non-motile spirochaetes; after longer periods free balloon-like forms occur. These various forms are shown in a diagram together with *T. pallidum* [the representation of the latter is far from accurate].

For cultural purposes modified Brewer's thioglycollate medium was found satisfactory; this consists of trypticase 15 g., disodium phosphate 7 g., dextrose 5 g., yeast extract 5 g., sodium thioglycollate 1·5 g. These are mixed and added to 1 litre of distilled water and the whole shaken several times over a period of half an hour. This mixture is brought gently to the boil and heated for 20 to 30 minutes to clarify the solntion. Finally, sterile serum previously heated to 60° C. for one hour is added, when the temperature has dropped to 60° C., to make a 10% concentration. (Spirochaetes do not grow in the absence of serum.) The medium was inoculated and the stoppered flask container placed on a magnetic stirrer base in the incubator at 3° C. for 4 to 5 days. Maximum growth gave a 286-fold increase in 5 days, the average division time being 8·8 hours for the first 48 hours

(compared with 30 to 32 hours for *T. pallidum*). Various methods were employed to estimate the number of spirochaetes; these included counting under the dark-ground microscope (a difficult and time-consuming method), turbidimetry, and micro-Folin and Kjeldahl nitrogen determinations, the results of which appeared to be comparable. The following quantitative measurements were recorded with mass cultivation: (1) 1×10^9 organisms contained 58·5 mg. nitrogen, and (2) 1×10^9 washed with saline and acetone and dried over P_2O_5 weighed 0·8 mg. *T. E. Osmond*

SYPHILIS

2961. **Comparative Study of Syphilis, Yaws, and Pinta.** (Étude schématique et comparative de la syphilis, du pian et du mal del pinto)
J. GRAU TRIANA. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **9**, 276–289, May–June, 1949. 2 figs., 38 refs.

The author, after a short historical note on pinta, describes its distribution, cause, mode of transmission, and lesions at various stages. He compares pinta in all its aspects with yaws and syphilis, illustrating his remarks with photographs and a comparative table. [This is an excellent résumé of the subject which ought to be read in the original.] *James Marshall*

2962. **Pulmonary Syphilis in a Moroccan.** (Syphilis pulmonaire chez un marocain)
—. DECROP and —. CABANIE. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **9**, 303–306, May–June, 1949. 2 figs., 3 refs.

A man aged 30 had a 6-months' history of cough and abundant expectoration. The right side of the chest was diminished in volume and the physical signs suggested a fibro-caseous tuberculosis. There was no fever, and tubercle bacilli were not found in the sputum or in stomach washings. Serum tests for syphilis gave positive results, but there was no abnormality in the cerebrospinal fluid. Treatment with neoarsphenamine caused a remarkable improvement, expectoration having ceased within a fortnight. The authors believe that the case was one of prenatal syphilis. [The radiological appearances are illustrated only by diagrams.]
James Marshall

2963. **Morphologic Changes in Syphilitic Lesions During the Jarisch–Herxheimer Reaction**
W. H. SHELDON and A. HEYMAN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **33**, 213–224, May, 1949. 3 figs., 22 refs.

This is a study of the histological changes caused by Jarisch–Herxheimer reactions, in the skin lesions of 29 cases of early and 2 cases of late syphilis. The specimens examined included one primary lesion, 28 secondary lesions, and 2 late nodular syphilides; 21 patients were treated with aqueous penicillin (80,000 units 3-hourly), 3 with daily injections of penicillin in oil and beeswax (600,000 units), and one with bi-weekly injections of the latter preparation. A single injection of " mapharsen " (oxophenarsine hydrochloride) was given to 9 patients and one of 2 ml. of sodium bismuth tartrate to one patient.

A definite clinical Herxheimer reaction was observed in 21 patients and in all but one of them histological changes were observed. This one patient had recurrent annular lesions and was treated with mapharsen. The histological changes during the reaction involve chiefly the small blood vessels and consist of an acute transient inflammation. Identical histological changes were produced by the authors and others in the skin lesions of syphilitic rabbits treated either with penicillin or mapharsen. The authors consider that these changes form the morphological basis of the phenomenon and are sufficient to account for the occasional disastrous complications which have occurred during the initial treatment of late syphilis. *G. L. M. McElligott*

2964. **The Jarisch–Herxheimer Reaction in Early Congenital Syphilis. A Study of Ninety-three Patients Treated with Penicillin Alone**
O. A. PARDO and H. A. TUCKER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **33**, 225–233, May, 1949. 5 refs.

The authors analyse the 45 febrile Herxheimer reactions which occurred in 93 children under 3 years of age who were treated with penicillin for congenital syphilis. No relation was noted between the incidence and strength of the reaction and age, race, sex, stage or type of infection, serological titre, or outcome. The type of penicillin (amorphous or crystalline G), within a dosage range of 250 to 7,600 units per kg. body weight, did not appear to be a factor. When it occurred, the reaction seemed to be entirely analogous to that seen in the adult with early acquired syphilis [and it is noted that the incidence is roughly the same]. Nine of the children died but in no case was death believed to be directly attributable to the reaction. *G. L. M. McElligott*

2965. **Penicillin Syphilotherapy Administered During Pregnancy. A Study of 149 Pregnancies During Which Penicillin was Given for Early Maternal Syphilis**
H. A. TUCKER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **217**, 157–161, Feb., 1949. 12 refs.

In this study of the treatment of syphilis with penicillin during pregnancy 70 (47%) of the 149 patients were suffering from primary or secondary syphilis and the remainder from early latent or early asymptomatic neurosyphilis of less than 2 years' duration. In all cases the penicillin was given in aqueous solution intramuscularly at intervals of 2 to 3 hours over a period of 7½ to 15 days, the total dose ranging from 600,000 to more than 5,000,000 units. Both amorphous and crystalline penicillin G were used, but the type of penicillin used did not seem materially to influence the results. Several of the patients, particularly those receiving less than 3,000,000 units of penicillin, were given concurrent

treatment with oxophenarsine hydrochloride (total dose approximately 300 mg.) and bismuth (total dose approximately 600 mg.).

Abortion occurred in 2 cases, one in the 15th and one in the 17th week of pregnancy, but in neither case was any evidence of congenital syphilis found in the foetus. There was one death, from sickle-cell anaemia, during the neonatal period. The surviving infants were fully examined at monthly intervals for 4 to 12 months or longer, quantitative serological tests being carried out in each case and the long bones being *x*-rayed in approximately 33%. Of the 146 infants 48 (33%) were serum-positive at, or within 1 month of, birth and in 12 (8%) radiological changes compatible with a diagnosis of healed syphilis were noted in the long bones, indicating that an infection *in utero* had probably been cured by treatment of the mother. In no case was treatment of the infant indicated during the first 4 months of life or longer, though in 2 cases serological reversal was delayed, and did not occur until 81 to 90 days in one case and 101 to 121 days after birth in the other. The author concludes that penicillin, followed by intensive serological and clinical study, is the current treatment of choice for the syphilitic pregnant woman.

[It is noted that 6 (4%) of the mothers needed re-treatment on account of relapse or reinfection during pregnancy and, in view of the possibility of this happening, it would still seem logical to treat all pregnant women with early syphilis *ad ultimam diem*.] *G. L. M. McElligott*

2966. **Observations on Penicillin-treated Cardiovascular Syphilis**

J. Edeiken, M. S. Falk, and H. P. Steiger. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **217**, 475–484, May, 1949. 2 figs., 13 refs.

A study of the literature suggests that there is a good deal of difference of opinion on whether it is safe to treat cases of advanced cardiovascular syphilis with penicillin. These authors describe the effect of treating 50 patients with either crude penicillin or crystalline penicillin G, in total doses varying from 1·2 to 9·6 million units. The patients included 23 with aortitis, 20 with aortic insufficiency, 5 with aneurysm, and 2 with aneurysm and aortic insufficiency; 40 were men and 10 were women: only 7 were under the age of 40 and the oldest was 69; 40% of the patients had received metal chemotherapy previously, but only 4 had done so within the previous 3 months; in 30 there was cardiac enlargement and in 14 there were cardiac symptoms before treatment was started; 38 patients had coincident neurosyphilis. The occurrence of Herxheimer reactions seemed to be unaffected by the size of the initial dose of penicillin; mild febrile attacks occurred in 7 patients, one complained of precordial constriction on the third day, and one had a recurrent attack of cardiac asthma on the third day, but in no case was it necessary to suspend treatment. In about half the cases electrocardiograms were taken at 3-day intervals, but significant changes in T waves were noted only in 8. Six patients had congestive heart failure before treatment but all tolerated penicillin, digitalis, and mercurial diuretics given concurrently. There were no instances of "therapeutic paradox" during the period of observation [length not stated]. It is concluded that penicillin is a valuable remedy for cardiovascular syphilis and that the danger of serious reactions is probably negligible. *T. E. Osmond*

2967. **Penicillin Treatment of Syphilitic Primary Optic Atrophy. An Interim Report**

J. V. Klauder and B. A. Gross. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **33**, 234–242, May, 1949. 2 refs.

Primary optic atrophy is probably the most serious and incapacitating complication of neurosyphilis. It may proceed slowly or rapidly to complete blindness or be arrested with only partial impairment of visual acuity. These intrinsic variations in behaviour and the relative rarity of cases make the assessment of a new form of treatment particularly difficult and open to error. The authors submit an interim report on some 56 cases treated with penicillin between April, 1944, and November, 1948. Thirty-four patients were treated with an aqueous solution of a partially purified sodium salt of penicillin alone (3-hourly injections for 7½ days to a total of 4·2 mega units). Subsequently, 22 patients were treated with 3·6 g. of crystalline penicillin G, injections being given every 3 hours for 7½ days (a total dose equivalent to about 6 mega units of amorphous sodium penicillin). In addition, eight to ten bouts of fever, usually malarial, were employed if the patient's physical condition warranted it. If the optic atrophy progressed unfavourably 3·6 g. penicillin G was given again, together with further fever therapy and metal chemotherapy.

Results were inconclusive and variable, some cases responding to little treatment while in others the condition progressed unfavourably after much more therapy. Some of the cases classified as "progressive" before treatment and "unchanged" after treatment may, with longer observation, have to be transferred to the "worse" group. [This factual report does not lend itself to abstracting; the further report promised on these patients after longer observation should be of greater interest and value.] *S. M. Laird*

2968. **Penicillin in Oil and Beeswax in the Treatment of Syphilis in Clinic Patients**

H. Eisenberg and F. Plotke. *American Journal of Medicine* [*Amer. J. Med.*] **6**, 449–452, April, 1949.

In February, 1947, a short-term ambulatory method of treatment of syphilis with penicillin in oil and beeswax was introduced under the Venereal Disease Control Programme of the Chicago Health Department. The first 1,000 cases treated on this basis are here analysed according to age group, diagnosis, and completion of treatment; results of treatment at follow-up are omitted. This ambulant treatment was intended primarily for untreated or inadequately treated late latent syphilis (596 cases) but other types of case were also included—for example, cases of neurosyphilis (249) and of syphilis in pregnancy (93).

The median age was raised to 38 years by the inclu-

sion of so many latent cases. The treatment consisted of daily injections of 450,000 units of penicillin in oil and beeswax over a period of 10 treatment days (omitting Saturdays and Sundays). In cases of neurosyphilis with group 2 and group 3 cerebrospinal fluid changes the course was extended to 15 treatment days (6,750,000 units), while cases of cardiovascular syphilis were treated with 100,000 units daily for 3 days, increasing to 200,000 units on the 4th and 5th days and to 300,000 units from the 6th to the 15th days.

About 86% of all patients completed the prescribed course of treatment; treatment was interrupted because of local or allergic complications in 2·8%, and because of intercurrent illness in 6%, 81·8% of these patients later completing a new treatment course. Only 125 patients (12·5%) disappeared and failed to complete treatment for unknown reasons. The authors conclude that this form of therapy is far superior, in respect of clinic attendance, to long-term chemotherapy, in which only 30% of patients complete the prescribed course.

S. M. Laird

2969. **Treatment of Syphilis with a Penicillin–Bismuth Mixture.** (Traitement de la syphilis par mélange penicilline-bismuth)

A. ALECHINSKY. *Archives Belges de Dermatologie et de Syphiligraphie* [*Arch. belges Derm. Syph.*] **5**, 100–104, April, 1949. 1 ref.

The method advocated for treatment of syphilis consists in giving a mixture of 2 ml. " retard " penicillin (600,000 units) and 2 ml. bismuth campho-carbonate (80 mg.) every day for a 30-day course. After a rest of a fortnight treatment begins again, and two or three courses are given, depending on the case. A few case histories are presented. *James Marshall*

2970. **Comparison of Results in the Treatment of Early Syphilis by Neoarsphenamine–Bismuth, Arsenoxide–Bismuth, and Combinations of Penicillin–Arsenoxide–Bismuth.** (Résultats comparatifs, dans le thérapeutique de la syphilis primosecondaire, des traitements par le novarbismuth, les arsénoxydes-bismuth et les combinations pénicilline-arsénoxydes-bismuth)

—. LAPIÈRE and —. FASSOTTE. *Archives Belges de Dermatologie et de Syphiligraphie* [*Arch. belges Derm. Syph.*] **5**, 70–84, April, 1949. 3 figs.

The schedules used for treatment of early syphilis consisted of: (1) 3 courses of neoarsphenamine (20 g. total) and bismuth and 2 courses of bismuth alone, lasting for 18 months altogether; (2) 5 months' treatment with bi-weekly injections of dichlorarsine (each of 60 to 100 mg.) with 8 injections of bismuth at the beginning and again at the end; (3) various combinations of penicillin, arsenoxide, and bismuth, one of which is comparable to the schedule (2) above with addition of 2,400,000 units of penicillin. Default was less common with the short courses of treatment than with long courses. Serious toxic reactions were definitely less common with the arsenoxides than with neoarsphenamine. Syringe-transmitted jaundice occurred in about 20% of cases in all groups. The addition of penicillin to the arsenoxide-bismuth combination improved results. The authors conclude that the short courses of treatment are only effective in the earliest cases and that advanced secondary syphilis should be treated with neoarsphenamine and bismuth. *James Marshall*

2971. **Rapid Treatment of Syphilis.** (Traitement mixte massif de la syphilis par pénicilline-arsénobenzol-bismuth)

P. POPCHRISTOFF, G. GHEORGHIEFF, and A. LEVCOFF. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **9**, 290–299, May–June, 1949. 4 refs.

The method of treatment of syphilis described is based on the assumption that, under the protection of penicillin, large doses of arsenic and bismuth may be injected in a very short time without danger, and that by employment of arsenic and bismuth it is possible to increase the bacteriostatic and bacteriolytic effects of minimal doses of penicillin. The schedule eventually adopted consisted of injections of 20,000 to 30,000 units of penicillin intramuscularly every 3 hours to a total of 500,000 to 600,000 units in 3 to 4 days; doses of neoarsphenamine, 0·15, 0·3, 0·45, and then 0·6 g. repeated, were also given every 6 hours (half an hour to one hour after a penicillin injection) to a total of 4·5 to 5·5 g. and 1 ml. bismuth every 6 hours to a total of 15 ml.

Five patients previously intolerant to neoarsphenamine tolerated the treatment without ill effects, and 3 cases in which there was relative resistance to standard treatment responded to the intensive method. Thirty-three patients, of whom 4 had neurosyphilis and the rest had early syphilis, were treated. The authors observe that a larger series and a longer follow-up period will be required before the value of this treatment can be assessed. *James Marshall*

2972. **Treatment of Early Syphilis with Penicillin Injection in Oil and Wax *U.S.P.* Report of One Hundred and Fifty-three Cases**

L. CHARGIN, N. SOBEL, C. REIN, and T. ROSENTHAL. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **59**, 595–605, June, 1949. 5 refs.

2973. **The Value of Diluted Antigen in the Wassermann Reaction**

R. F. JENNISON, J. B. PENFOLD, and J. A. FRASER ROBERTS. *Journal of Clinical Pathology* [*J. clin. Path.*] **2**, 129–133, May, 1949. 3 figs., 5 refs.

2974. **Gumma of the Heart. A Report of Three Cases**

S. N. KOTHARE. *Indian Medical Gazette* [*Indian med. Gaz.*] **84**, 137–139, April, 1949. 8 refs.

2975. **The Rate of Multiplication of *Treponema pallidum* in Normal and Immune Rabbits**

M. C. CUMBERLAND and T. B. TURNER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **33**, 201–212, May, 1949. 2 figs., 13 refs.

See also Section Pharmacology and Therapeutics, Abstract 2712.

Genito-Urinary Disorders

2976. **Coliform Infection of the Urinary Tract**
P. M. COLEMAN and S. TAYLOR. *Journal of Clinical Pathology* [*J. clin. Path.*] **2**, 134–137, May, 1949. 16 refs.

This paper, from Bolton, Lancashire, records the types of coliform organisms found in 100 consecutive cases of urinary infection. The cases were divided into two groups. Group I included cases of pyelitis and cystitis without a gross surgical lesion of the urinary tract (mostly in women, and mostly associated with pregnancy). Group II consisted of cases secondary to an obstructing or other pathological lesion (mostly in men with enlargement of the prostate or paraplegia).

In 48 out of 60 cases in group I *Bacterium coli* was grown in pure culture. *Proteus vulgaris*, *Bact. aerogenes*, and Gram-positive cocci were infrequent. In group II, the reverse was found to be the case, *Bact. coli* being relatively uncommon (7 strains out of 56). Its place was taken in roughly equal proportions by *Proteus vulgaris*, *Proteus morgani*, *Bact. aerogenes*, and Gram-positive cocci. A pure culture was most unusual.

These findings are of great importance as regards treatment. Bacteriostatic concentrations of penicillin or sulphonamides in urine against *Bact. aerogenes* or *Proteus morgani* cannot be obtained. Thus for cases in group II streptomycin is the only drug which will produce bacteriostasis of the mixed collection of organisms usually present, and this only for a short time. Its use is therefore confined to producing a temporary clear field for a surgical procedure. *F. B. Cockett*

KIDNEY

2977. **The Cause of Experimental Anuria with a Low Blood Chloride.** (Le déterminisme de l'anurie hypochlorémique expérimentale)
E. DE MUYLDER and J. SONNET. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **78**, 595–612, April, 1949. 3 figs., 9 refs.

Anuria produced in rabbits by intravenous injection of hypertonic glucose solution is primarily due to the fall in concentration of the sodium ion in the blood. If the anuria were simply due to loss of water owing to decreased tubular reabsorption as a result of inhibition of the posterior lobe of the pituitary, then intravenous injection of isotonic glucose should be as effective in restoring urine flow as isotonic saline. However, diuresis was re-established by injecting isotonic saline, which restores colloid osmotic pressure to normal and tends to re-establish ionic equilibrium, whereas isotonic glucose solution was ineffective in spite of its equivalent effect on colloid osmotic pressure. The urinary chloride concentration during the saline-induced diuresis was low. The potassium level in the blood was already raised in these animals and injection of potassium chloride caused death. It appears that the sodium ion was of greater importance than the chloride ion. The re-establishment of urine flow was due to increased glomerular filtration but unrelated to changes in blood pressure. It was also shown that reduction in salt concentration without altering the colloid osmotic pressure, by injecting isotonic glucose solution into normal rabbits, was accompanied by a fall in glomerular filtration rate, measured by the inulin clearance. The diuresis produced by glucose was greater than that produced by saline since tubular reabsorption was much less after the glucose, a difference at least partly explained by an action via the posterior pituitary. Apart from the diuretic effect, this effect of isotonic glucose is quite comparable to that found in experimental anuria. Filtration and reabsorption are reduced; tubular reabsorption of potassium is almost nil, while that of sodium and chloride is almost complete. In some extreme cases there is evidence that potassium may even be secreted by the tubules. The logical treatment of this experimental anuria is by injection of isotonic or slightly hypertonic sodium chloride solution.
Derek R. Wood

2978. **The Effect of Exercise on the Renal Mechanism of Electrolyte Excretion in Normal Subjects**
A. A. KATTUS, B. SINCLAIR-SMITH, J. GENEST, and E. V. NEWMAN. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **84**, 344–368, April, 1949. 13 figs., 21 refs.

This paper reports the effect of moderate exercise on glomerular filtration rate (G.F.R.), urine flow, and the excretion of sodium, chloride, potassium, and phosphate in normal subjects. Since water diuresis was used to increase the accuracy of urinary collection, control tests were carried out, and it was found that the G.F.R. and electrolyte excretion were not significantly altered by ingestion of a litre of water. Quiet standing also did not alter these aspects of renal function, but this finding does not conflict with the known effect of the completely passive erect posture, with a perineal support, in lowering G.F.R. and renal blood flow. Good agreement was found between the clearance of inulin and of endogenous creatinine, and the creatinine clearance was used as the measure of G.F.R. in most of the experiments on exercise, which consisted of walking at 3 miles (4·8 km.) an hour on a treadmill for periods varying from 20 minutes to an hour. In most experiments, the G.F.R. did not change during exercise of this severity, but in two experiments there was some fall in the G.F.R. The exercise was mild, and this result does not conflict with findings in other studies that severe exercise lowers the G.F.R. Exercise was attended by a fall in urine flow, and chloride excretion was decreased, in contrast to experimental pituitary antidiuresis in which the chloride output increases. The fall in excretion of sodium and chloride was not related to changes in G.F.R., nor was it related to the pre-exercise level of sodium excretion. The depression of sodium excretion lasted on an

average for 37 minutes from the end of exercise. Potassium and phosphate excretion showed no systematic change during exertion. The mechanism of sodium and chloride retention " will be the subject of further study in normal subjects ". *D. A. K. Black*

2979. **The Renal Mechanism of Electrolyte Excretion and the Metabolic Balances of Electrolytes and Nitrogen in Congestive Cardiac Failure: The Effects of Exercise, Rest and Aminophyllin**

B. SINCLAIR-SMITH, A. A. KATTUS, J. GENEST, and E. V. NEWMAN. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **84**, 369–394, April, 1949. 12 figs., 23 refs.

Observations on the effect of exercise and of aminophylline administration on renal clearance were made in 3 patients at different stages of congestive heart failure. In previous work it was found that exercise depressed excretion of sodium and chloride in normal people, even without any fall in glomerular filtration rate (G.F.R.) Exercise in patients with cardiac failure had a similar, if not a greater, effect in depressing salt excretion. The ratio of clearance of sodium to clearance of creatinine fell, showing that tubular reabsorption of sodium had increased, independent of any change in G.F.R. In the patients with heart disease, but not in the normal persons, there was a considerable fluctuation in the " control " values for G.F.R., and a tendency for the G.F.R. to drop significantly during exercise. This fall in G.F.R. did not account for more than a part of the diminution in salt excretion, the rest being caused by increased activity of the tubules in reabsorbing salt. The mechanism of this change is not known. By contrast, aminophylline depressed tubular reabsorption of salt so that excretion of sodium and of chloride increased. In some patients this action accounted for the whole effect of aminophylline on salt excretion, since the G.F.R. did not change. In other patients, with a greater rise in venous pressure, the action of aminophylline in increasing cardiac output contributed to the enhanced salt excretion, since the G.F.R. rose in these patients and so more salt was filtered. An interesting finding was that salt retention in the patient with heart failure was often associated with a high " filtration fraction " (ratio of inulin clearance to *p*-aminohippurate clearance). *D. A. K. Black*

2980. **Transmural Migration of Intestinal Bacteria During Peritoneal Irrigation in Uremic Dogs**

F. B. SCHWEINBURG, H. A. FRANK, E. D. FRANK, F. HEIMBERG, and J. FINE. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **71**, 150–153, May, 1949. 4 refs.

Peritoneal irrigation was carried out repeatedly in 3 normal dogs and in 18 which were uraemic after bilateral nephrectomy, 1½ to 3 litres of sterile modified Locke solution with gelatin of *p*H 7·2 to 7·9 being used on each occasion, with every precaution against contamination. Samples of the fluid from the needle, of fluid aspirated after a few minutes, of residual fluid aspirated after 12 hours, and swabs from the skin were cultured in various media. The normal dogs received 10 to 40 litres in 11 to 16 days, of which 30 litres was recovered by aspiration from one, but very little from the others. Of the uraemic dogs, 11 were treated similarly, but consumed no food or water post-operatively, 3 had a sterile foreign body placed in the peritoneum, 4 were given 0·1 g. of streptomycin and 1·0 g. of phthalylsulphathiazole by mouth for 4 to 5 days before nephrectomy. In the normal dogs no peritoneal contamination occurred, nor in 10 rabbits treated similarly. Of the first group of 11 uraemic dogs, 2 died within 4 days of operation and the remainder, which survived 5 to 16 days, all developed a *Bacterium coli* infection of the peritoneal fluid, 7 with *Bact. aerogenes* in addition. The second group did not differ from these, but in the last group stool culture was negative and peritoneal infection did not occur. A weakening of the integrity of the gut wall in uraemia is held to be the cause of the transmural migration of bacteria. It can be prevented by suitable oral therapy designed to sterilize the gut. *James D. P. Graham*

2981. **Autoantibodies in Human Glomerulonephritis**

K. LANCE, M. M. A. GOLD, D. WEINER, and V. SIMON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **28**, 50–55, Jan., 1949. 15 refs.

Various investigators have suggested an organ-specific antigen–antibody reaction as the aetiological agent in nephritis. Their work is reviewed in this article and experiments are described in which a suspension of collodion particles coated with a 1 in 60 dilution of an extract of homologous kidney (preferably infant or foetal) was used as antigen. [For complete details of the method of preparation of the antigen, the original paper should be consulted.] The antigen was mixed with doubling dilutions of the serum to be tested and allowed to stand for an hour. The mixture was then centrifuged and resuspended. A positive reaction was shown by the presence of discrete particles in a clear fluid and a negative reaction by the persistence of a milky fluid. Absorption of the sera with human liver extract or human mixed erythrocytes did not affect the specificity of the reaction.

Although serum from 23 patients with glomerulonephritis gave a persistently positive reaction (titre greater than 1 in 10 in more than 60% of tests) in 78% of cases as against 6% in the control group (68 patients) it was found that the serum of patients with less than one year's history gave positive results in only 58% of cases, whereas positive results were obtained in all cases in which there was a longer history. The average titres were: in all cases of nephritis, 1 in 623; in early cases, 1 in 918; in late cases, 1 in 327; and in controls, 1 in 78.

The authors point out that the tests are difficult to carry out and are very delicate. They discuss the reasons for the variations in titre in individual cases, the effect of measles on the titre, and the possible relation between auto-antibody titres and streptolysin titres. [This important and interesting paper should be read in full.] *J. Maclean Smith*

See also Section Endocrine Disorders, Abstract 2929.

Locomotor Disorders

2982. **Pathogenesis of Concurrent Eye and Joint Diseases**
E. GODTFREDSEN. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **33**, 261–270, May, 1949. 37 refs.

As the aetiology and pathogenesis of many cases of iridocyclitis, scleritis, and phlyctenular conjunctivitis are still obscure, and as these diseases are frequently met with in association with diseases of joints, the author analyses the nature and frequency of eye symptoms in joint diseases in an attempt to elucidate the underlying pathology.

The medical or rheumatic joint diseases complicated by eye symptoms can be divided into two groups—acute and chronic. Of the first group, rheumatic fever is complicated by conjunctivitis in 5 to 10% of cases, and by iritis in 4 to 5%; gonorrhoeal arthritis, by conjunctivitis in 10% and iritis in 5%; Reiter's disease, by conjunctivitis in 80% and iritis in 10%. Of the second group, primary progressive chronic polyarthritis is accompanied by iritis in 2 to 5% of cases, and by the sicca syndrome in a further 10%; Still's disease, by iritis in 20%; and ankylopoietic spondylo-arthritis, by iritis in 15 to 50%.

In Denmark there are 4,000 fresh cases of rheumatic fever annually and 300 to 400 fresh cases of primary chronic polyarthritis. All other joint diseases are far less frequent, but Reiter's disease has been observed with increasing frequency. The eye symptoms in these joint diseases can be divided into three distinct groups: (1) endogenous conjunctivitis, including episcleritis and scleritis; (2) iritis and iridocyclitis; and (3) the sicca syndrome.

The pathogenesis of the joint diseases is not yet fully elucidated. Rheumatic fever is probably an allergo-toxic reaction to infection with haemolytic streptococci —a hypothesis supported by an increased antistreptolysin titre in 80% of cases. The aetiology of Reiter's disease is still obscure, but a virus may be implicated. The three chronic joint diseases are presumably infective with an allergo-toxic pathogenesis. The primary infective agent giving rise to the allergo-toxic reaction in the two groups is clear only in rheumatic fever and gonorrhoeal arthritis. It is assumed that the pathogenesis of the eye signs is the same as that of the joint symptoms and is of an allergo-toxic nature. This hypothesis is supported clinically in that phlyctenular conjunctivitis and episcleritis are found in recognized allergic conditions, such as serum disease and sulphonamide and tuberculin allergy. The histopathological picture of phlyctenular conjunctivitis is the same in both groups.

It is concluded that in those of the rheumatic joint diseases which belong to the infective type, arthritis is sometimes associated with eye symptoms, chiefly of an allergo-toxic nature. The pathogenesis is presumably the same for the eye and the joint disease. The allergo-toxic basis is supported clinically by the resemblance in the symptomatology of the rheumatic group to that of a group, generally presumed to be allergo-toxic, affecting the eye, joints, skin, and mucous membranes.

S. J. H. Miller

2983. **Observations on Heberden's Nodes.** (Contributo alla conoscenza dei noduli digitali di Heberden)
A. ROBECCHI and F. PINO-SACCA. *Revue du Rhumatisme* [*Rev. Rhum.*] **16**, 132–141, April, 1949. 11 figs., 5 refs.

In previous papers the authors published the results of their investigations on the problem of Heberden's nodes from the clinical point of view, based on 2,000 personal observations. In this paper they report some anatomical findings. Their examinations were carried out at the Medical Clinic of the University of Turin. They studied nine fingers on which Heberden's nodes were present. The fingers were removed from the bodies at necropsy and the authors knew nothing of the cause of death of these patients. No family history could be found in any of the cases. The fingers were fixed in formalin, decalcified in 3% nitric acid, dehydrated in alcohol, transferred to cedarwood oil, and enclosed in formalin. Longitudinal sections were stained with haematoxylin-eosin, Weigert's stain for elastic fibres, and Mallory's original stain, and in some cases with Schmorl's thionin. The histological changes were identical with those of osteo-arthritis.

E. Forrai

2984. **A Factor Determining the Location of Pseudo-fractures in Osteomalacia**
M. LE MAY and J. W. BLUNT. *Journal of Clinical Investigation* [*J. clin. Invest.*] **28**, 521–525, May, 1949. 5 figs., 13 refs.

The authors have been dissatisfied with the usual explanations—such as muscle strain and minor trauma—given for the development of pseudo-fractures in osteomalacia. They have accordingly developed a new and anatomical explanation which accounts for the common sites of development of these lesions. Four cases of their own and a larger number from the literature are reviewed, and it is shown that the sites of development of these pseudo-fractures coincide in most cases with points where arteries are running across the bone and in direct contact with it. They therefore suggest that the pressure of these arteries causes an erosion of the bone at the point of pressure. Normally this would lead to callus formation and recalcification, but in osteomalacia any callus formed tends to remain uncalcified.

[This appears the most satisfactory explanation of the mechanism of pseudo-fracture formation which has yet been put forward.]

C. L. Cope

2985. **The Potential Reversibility of Rheumatoid Arthritis**
P. S. HENCH. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **8**, 90–96, June, 1949. 19 refs.

Neurology

2986. **Analysis of Electroencephalographic Findings in Forty Cases of Verified Brain Tumor. I. Electroencephalographic Findings in Meningiomas**
H. M. CUNEO, C. W. RAND, and H. SJAARDEMA. *Bulletin of the Los Angeles Neurological Society* [*Bull. Los Angeles neurol. Soc.*] **14**, 1–22, March, 1949. 10 figs.

This paper is limited to the presentation of 10 examples of meningioma. In each case there is a short summary of the history, neurological and laboratory findings, electroencephalographic changes, the results of ventriculography, and the finding at operation. The nature of all the tumours was verified histologically. Electroencephalography was of no help in locating the tumour in 3 cases and gave an inaccurate result once.

[This first paper contains neither conclusions nor summary; no doubt both will appear at the end of the series.] *Hugh Garland*

2987. **The Electroencephalogram Obtained by Direct Leads at Operation.** (Биотоки мозга человека при непосредственном отведении во время операции)
L. A. KOREISHA and V. E. MAIORCHIK. Вопросы Нейрохирургии [*Vop. Neirokhir.*] **13**, No. 2, 3–10, March–April, 1949. 4 figs.

The authors have studied the pathological physiology of the human brain in 25 cases by recording an electroencephalogram (E.E.G.) directly from the brain during operation in 18 cases of brain tumour, 3 of arachnoiditis, and 4 of traumatic epilepsy. A silver wire electrode 7 to 8 cm. long and 0·5 mm. in diameter was used. The E.E.G. from large areas of the cortex was recorded by the unipolar method and from small areas by the bipolar method. According to the authors the direct method of recording the E.E.G. has the following advantages: (1) The extent of the pathological process can be shown. (2) There is no interference from muscles and blood vessels. (3) The E.E.G. can be taken from deeper layers of the brain. (4) The E.E.G. can be taken under local and general anaesthesia. The E.E.G. taken during operation by the direct method was similar to the post-operative one only during the first 3 to 5 minutes. The E.E.G. was different when taken over the pathological tissue, over adjacent areas, and over zones 4 to 5 cm. away except in cases of malignant infiltrating tumours where it was the same over the whole of the exposed area. Over the pathological tissue α-waves were not well defined, over the adjacent zones α-waves were smaller and alternated with δ-waves and fast potentials. Farther away there was at first normal α-rhythm, the amplitude of which diminished during operation. During operations for traumatic epilepsy and arachnoiditis slow waves were frequently observed—this observation seems to rule out the specificity of slow waves in localized processes such as tumours. Fast potentials are not necessarily diagnostic of epilepsy.

Seven patients were observed during general anaesthesia with " hexenal " (an " evipan " analogue). As hexenal is supposed to block the thalamic centres it was possible to study the impulses due to the cortex alone. Three phases were observed: (1) In the first 2 to 3 minutes there was a rapid increase in the amplitude of α-waves. (2) Slow waves appeared and increased in number, and normal α-waves gradually disappeared, in the period of deepest sleep; the appearance of slow waves was thought to be due to alteration of functional activity of the cortex by hexenal. Interpretation of the E.E.G. in the third phase is uncertain, but there were slow waves in groups with intervals.

Summarizing the evidence, the authors point out that slow pathological waves of varying duration, and fast high-voltage potentials, are not specific features of any disease of the brain. They represent a reaction of the cortex to an interruption of its physiological function either through a pathological focus, during operation, or during a certain phase of anaesthesia.

N. Chatelain

2988. **Unilateral Prefrontal Lobotomy for Relief of Intractable Pain. Preliminary Report of Eight Cases**
P. J. VOGEL and C. D. HJARTARSON. *Bulletin of the Los Angeles Neurological Society* [*Bull. Los Angeles neurol. Soc.*] **14**, 32–39, March, 1949. 2 refs.

CENTRAL NERVOUS SYSTEM

2989. **Observations on the Pathology of Hydrocephalus**
D. S. RUSSELL. *Medical Research Council. Special Report Series* [*Spec. Rep. Ser. med. Res. Counc., Lond.*] No. 265, 1–138, 1949. 90 figs., bibliography.

From this study the author has been able to discount completely the old conception of an " idiopathic " form of hydrocephalus by showing that in every case of the so-called " idiopathic " variety it is possible to demonstrate some kind of obstruction. Attention is also directed in the preface to the importance of hydrocephalus after various forms of meningitis, in view of the fact that the mortality rate of meningitis, especially of the suppurative variety, has been greatly reduced by modern chemotherapy. Early recognition and efficient treatment of meningitis is urged in order that the subsequent development of hydrocephalus may be minimized; otherwise, although lives are saved which would formerly have been lost, the incidence of residual lesions such as hydrocephalus may be increased rather than reduced.

After a historical introduction and a description of the mechanism of production of hydrocephalus, the latter is considered under the recognized pathological headings of malformations, inflammations, and neoplasms. In the section on maldevelopment the term

"atresia" of the aqueduct is shown to be incorrect, because the word "atresia" implies complete non-patency. In 10 cases of so-called "atresia" the author found that at no point had the lumen disappeared completely, two distinct channels representing the aqueduct being invariably present. The term "forking" of the aqueduct is therefore suggested instead of "atresia". Much of the section on malformations is devoted to a detailed description of the Arnold-Chiari malformation associated with meningo-myelocele and hydrocephalus. In this malformation a tongue-like prolongation of the cerebellum (described by Arnold) overlaps and is bound down to a much elongated medulla (described by Chiari). These two components enclose a correspondingly elongated fourth ventricle. Hydrocephalus accompanied this malformation in every case investigated by the author.

Gliosis of the aqueduct is considered in a separate section, where emphasis is laid on the distinction between true gliosis of the aqueduct and a fibrillary astrocytoma arising in the quadrigeminal plate. The latter may, from its situation, prove fatal before the essential characteristics of the tumour are obvious, and it may simulate gliosis of the aqueduct. In true gliosis of the aqueduct there is a dense overgrowth of the subependymal neuroglia which gives rise to almost complete occlusion of the aqueduct with gross dilatation of the third and lateral ventricles. Theories of causation of gliosis of the aqueduct are fully and clearly discussed [but the author does not disclose her personal views.]

The occurrence of haemorrhage into the meninges in relation to the development of internal hydrocephalus is given due prominence, and rarities such as cysticercosis of the brain which may produce a hydrocephalus are mentioned with illustrative cases.

In the section on inflammations, hydrocephalus after pyogenic infections is discussed at some length; the initial illness may have been one of the respiratory or intestinal tract with minimal, and perhaps unrecognized, infection of the meninges. Syphilis, formerly considered to be one of the main causes of hydrocephalus in adult life, is at the present time a very rare cause. Only one such case, and that without confirmatory clinical evidence, is described in this series. Dural sinus thrombosis and thrombophlebitis, which have been associated with the condition of so-called "otitic" hydrocephalus, are discussed in detail, and the evidence for and against development of hydrocephalus as a result of dural sinus thrombosis is carefully weighed.

An account is given in the section on neoplasms of all the various tumours which may from their situation cause dislocation of the ventricular system and, by occlusion, produce hydrocephalus. Numerous examples, illustrated by case notes and excellent photographs, are given.

The concluding section on the anatomical effects of hydrocephalus deals with the general and local effects. The most interesting observation has been made that in chronic hydrocephalus, from whatever cause, the ependyma of the ventricles is often studded with tiny granulations, the so-called "granular ependymitis". This histological finding has, in the past, been considered to be pathognomonic of syphilis and generally to be found in general paralysis. The author has now shown that granular ependymitis is non-specific and may be found not only in any chronic inflammatory condition but also in the hydrocephalus associated with cerebral tumours. She suggests that its production is mechanical rather than inflammatory.

[Many well-reproduced photographs illustrate the monograph and enhance its interest. The literature of neuropathology is enriched by this contribution to the understanding of a difficult and important subject.]

Ruby O. Stern

2990. **Cytochrome C Therapy of Tissue Anoxia in a Case of Hepatolenticular Degeneration**

S. ZELMAN and T. GILBERT. *Archives of Internal Medicine* [*Arch. intern. Med.*] **81**, 485–500, April, 1948. 4 figs., 14 refs.

A case of hepato-lenticular degeneration with tissue anoxia treated with cytochrome C is described.

In May, 1943, the patient fell ill with a condition diagnosed as influenza. Subsequently he lost weight, and complained of pains in the chest and limbs and tremor of the hands. In January, 1946, because of fever and weakness he was compelled to abandon his work. Difficulty in speaking developed with tremor of the left hand, poverty and slowness of movement, and drooling. In September, 1946, at the age of 30, he had immobile facies and general slowness and lack of movement with a bilateral static tremor. There was cog-wheel rigidity but little weakness; the reflexes were exaggerated and the plantar responses extensor. In addition the liver was smooth and enlarged, the skin pigmented, the fingers clubbed, and the ankles oedematous. The heart and lungs were normal. After admission bleeding from the gums and petechiae appeared. The venous blood was intermittently bright red and later Kayser–Fleischer rings developed.

The erythrocyte count was 4,000,000 per c.mm. with 12·5 g. of haemoglobin per 100 ml. The sternal marrow was normal. The ascorbic acid concentration in plasma was normal, vital capacity 100%, and basal metabolic rate −20%. The oxygen level in venous blood was 15 volumes per cent. when the blood was red and 12 volumes when it was blue, the carbon-dioxide combining power being respectively 44 and 53 volumes per cent. Venous circulation time was normal. Kepler's test was negative and there was no evidence of heavy metal intoxication or of porphyrinuria. Skin biopsy examination showed a non-ferrous pigmentation of the basal layer of the epidermis.

The high oxygen content of venous blood in the presence of a normal circulation time was considered to indicate a histotoxic type of anoxia. An attempt was made to remedy the defect in the supply of oxygen to the cell by administration of cytochrome C prepared from equine myocardium. The patient was given 80 mg. or more intramuscularly each day from Nov. 29, 1946, together with 3 g. of sodium succinate, which also participates in oxidative metabolism, and large amounts of vitamin-B complex. Clinical improvement was noted

within a few days and by the end of 2 months the patient spoke well, walked unassisted, and had no tremor or cog-wheel rigidity, though some plastic rigidity remained. The oedema subsided, the pigmentation lessened, and the drooling ceased. The bleeding time fell to normal (from 6 to 3 seconds). The basal metabolic rate rose to normal and the acid-soluble organic phosphate level in serum rose from 0·6 to 1·1 mg. per 100 ml. The venous blood became blue or blue-black with oxygen levels of 6, 10·6, 8·3, and 3·8 volumes per cent. and arterial oxygen levels of 16·2, 14·8, and 14·1 volumes per cent. The arterio-venous oxygen difference, which before therapy varied from 1·3 to 3, rose to 6·5, a figure higher than the calculated normal of 5.

No side-effects were observed except an eosinophilia which increased to 46% by March 5, 1947, and a transient haemolytic reaction. Therapy was stopped on March 20 with the intention of later employing cytochrome prepared from beef muscle. Within a few days haemorrhagic manifestations and oedema appeared, the basal metabolic rate fell to −13%, the acid-soluble organic phosphorus level in serum to 0·8 mg. per 100 ml., oxygen levels in venous blood became 7·5, 13·7, 11·8, 10·7, and 9·8 volumes per cent. Pneumonia developed and on April 10 therapy was re-started with 150 mg. of beef cytochrome C intramuscularly daily. The patient's condition continued to deteriorate, however, and on April 24 death occurred.

Necropsy revealed a periportal cirrhosis with multilobular regeneration, degeneration of the lenticulostriate nuclei, fatty degeneration of the myocardium, parenchymatous degeneration and tubular necrosis of the kidney, fibrosis of the spleen, hyperplasia of the bone marrow, and lipid pneumonia. It seems, therefore, that in this case hepato-lenticular degeneration was associated with a failure in the oxidative processes in the tissues. Both oxidation and the clinical condition were favourably influenced by cytochrome C therapy. Necropsy revealed a surprising degree of hepatic regeneration and bone-marrow hyperplasia, considered to be a result of the increased oxidation induced by the cytochrome. *Fergus R. Ferguson*

2991. **The Uptake of Radioactive Phosphorus by Malignant Brain Tumors**

T. C. ERICKSON, F. LARSON, and E. S. GORDON. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 587–591, May, 1949. 10 refs.

At the Departments of Neurosurgery and Medicine, University of Wisconsin, the authors have investigated the possibility of producing significant intracellular concentrations of radioactive phosphorus in malignant brain tumours. Sodium phosphate, containing radioactive phosphorus (P^{32}), was given to patients by injection into the median basilic vein, the carotid artery, or locally into the tumour. At varying times after the injection tissue was obtained for biopsy, both from the tumour and from adjacent normal tissue, and immediately frozen by immersion in liquid air. In order to trace the distribution of the phosphorus within the tissue components, chemical fractionation studies were carried out according to the technique of Schneider (*J. biol. Chem.*, 1945, **161**, 293; 1946, **164**, 747), in which the total tissue phosphorus is divided into four fractions—acid soluble, alcohol-ether soluble, ribose nucleic acid, and desoxyribose nucleic acid. Tests of tissue activity were carried out on the gross specimen and on each of these fractions individually. In every case, the concentration of radioactive phosphorus in the tumour tissue exceeded that in normal brain tissue, the ratio ranging between 1·6 to 1 and 29 to 1. The highest ratio following intravenous injection was 19 : 1. This selective absorption was also observed in the chemical fractionation studies, in which a small but significant concentration of radioactive phosphorus was found in the nucleoprotein of both cytoplasm and nucleus.

The therapeutic implications of these findings are discussed. It is possible that, with their high metabolic activity, growing neoplastic cells in malignant brain tumours may show a greatly augmented phosphorus metabolism, leading eventually to a sharp rise in the more stable nuclear fraction. Repeated administration of small doses of radioactive phosphorus would thus produce a higher concentration in the desoxyribose nucleic acid fraction, with a more sustained therapeutic radiation effect than could be obtained from a single large dose. *A. S. McLean*

2992. **Prognosis in Initial Stage of Disseminated Primary Demyelinating Disease of Central Nervous System**

P. THYGESEN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **61**, 339–351, April, 1949. 5 refs.

Patients with disseminated sclerosis and acute disseminated encephalomyelitis, who had been examined at the two largest neurological clinics in Copenhagen within one year of the initial appearance of symptoms, were followed up for from 8 to 15 years. For the purpose of this investigation a pre-existing retrobulbar neuritis was not considered as an initial symptom. The criteria adopted for the diagnosis of disseminated sclerosis were: (1) neurological symptoms, especially those referable to the pyramidal tracts in a patient in whom retrobulbar neuritis had previously occurred or was simultaneously present; (2) remitting symptoms due to lesions of pyramidal tracts, including tracts mediating sphincter control, when no other cause could be found; (3) remitting paraesthesiae when no other cause could be found; (4) symptoms referable to the pyramidal tracts, regardless of earlier symptoms of retrobulbar neuritis and the remitting or non-remitting character of the symptoms, when no other cause could be found; and (5) monosymptomatic forms of the disease which could not be shown to be due to syphilis or arteriosclerosis and which were not associated with notable changes in the cerebrospinal fluid. The author admits that there may be no distinct clinical or pathological difference between disseminated encephalomyelitis and disseminated sclerosis, but the former diagnosis was made in cases with immediately preceding infection, pyrexia, and acute onset with rapid progress of symptoms and prominent symptoms of an encephalitic

condition. Initially there were 84 cases of disseminated sclerosis, 29 of acute disseminated encephalomyelitis, and 31 cases in which a tentative diagnosis of disseminated sclerosis was made.

Of the 29 patients with disseminated encephalomyelitis, 5 died—4 within one year of the onset—and 13 remained free from symptoms after the first 12 to 18 months of the disease. In 7 patients typical disseminated sclerosis developed, and 4 cases were later diagnosed as of lethargic encephalitis. Of the 31 cases with a tentative diagnosis, in 19 a firm diagnosis of disseminated sclerosis was made later, while in the others this diagnosis was subsequently discarded.

The 110 patients with a firm diagnosis of disseminated sclerosis were studied for from 8 to 15 years after their initial admission. One-third died within 15 years, 13% were practically or completely symptom-free after 8 to 15 years, and in 12% there had been long remissions or the disease had become stationary at an early stage so that the patients were capable of working after 8 to 15 years; in fact, the disease had run a benign course over this period in one-quarter of the cases. The author found that where the disease had a relatively benign course it had almost invariably an acute or subacute onset followed by a totally or partially remittent course in the first year. In practically all the cases with an insidious onset and steady progression within the first year the disease had an unfavourable course. The cerebrospinal fluid gave no prognostic indications. In general the course of the disease was more benign in the higher age groups.

[This is an important study of the prognosis of disseminated sclerosis, and there are many interesting observations which cannot be included in an abstract. It should be read in conjunction with the report of a follow-up of a considerably larger number of cases in Sweden by Muller (*Acta med. scand.*, 1949, **133**, Suppl. 222).] *J. W. Aldren Turner*

2993. **Atypical Syndromes Produced by Extramedullary Tumor of Cervical Portion of Spinal Cord**
B. C. MEYER and B. D. FINE. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **61**, 262–274, March, 1949. 18 refs.

PERIPHERAL NERVOUS SYSTEM

2994. **Primary Optic Atrophy in Von Recklinghausen's Disease. (Multiple Neurofibromatosis)**
E. DRESNER and D. A. D. MONTGOMERY. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **18**, 93–104, April, 1949. 4 figs., 45 refs.

The association of primary optic atrophy with von Recklinghausen's disease is a rare occurrence, but cannot be regarded as fortuitous. The optic atrophy has been ascribed to " neurofibromatosis " of the optic nerve or chiasma, but the author's review of the literature of the condition suggests that the tumour is nearly always a primary glioma. In 41 out of 46 cases previously recorded in which a histological examination was made, 35 (85%) had a glioma of the optic nerve or chiasm. The authors add an account of 3 cases of their own, 2 of which occurred in uniovular twins, a hitherto unrecorded hereditary manifestation. Their third case came to necropsy, and histological examination of the left optic nerve revealed a gliomatous tumour just distal to the chiasma.

The clinical, diagnostic, and hereditary aspects of the syndrome are briefly reviewed and the authors suggest that if its occurrence is borne in mind a careful examination for signs of von Recklinghausen's disease in patients with optic atrophy may reveal the association more frequently. *J. MacD. Holmes*

2995. **Pathogenesis and Prophylaxis of Post-diphtheritic Polyneuritis.** (Zur Pathogenese und Prophylaxe der postdiphtherischen Polyneuritis)
R. GAUPP. *Nervenarzt* [*Nervenarzt*] **20**, 227–229, April, 1949. 9 refs.

The author discusses the significance of recent observations on post-diphtheritic polyneuritis. An allergic serous inflammation of the spinal meninges always precedes post-infective polyneuritis, and shows itself by a cell-protein dissociation in the cerebrospinal fluid though variations in the fluid cannot be correlated with clinical findings. Where there is a long interval between infection and polyneuritis external factors, especially bodily overactivity, play an important part in precipitating the latter. This is also a factor in experimental polyneuritis and acute anterior poliomyelitis; it may be supposed that these factors lead to metabolic changes, which reduce the resistance of peripheral nerves to toxins. The finding of a cell-protein dissociation indicates that there is a danger of development of polyneuritis. It is, however, probable that the nervous complications of infectious disease may be limited to a serous meningitis without going on to polyneuritis. Experience shows that with timely recognition of danger by a study of the cerebrospinal fluid, polyneuritis may be prevented by strict rest in bed. *W. Forster*

2996. **Hypertension as a Release Phenomenon in Polyneuritis.** (Über Entzügelungshochdruck bei Polyneuritis)
H. LAMPEN. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **74**, 536–540, April 29, 1949. 13 refs.

The author reports 10 cases of peripheral neuritis of varied aetiology in which there were transient hypertension and tachycardia. In most cases the ninth and tenth cranial nerves were involved, and the fall in blood pressure coincided with the recovery of function of these nerves. It is suggested that this cardiovascular change is a release phenomenon due to toxic or inflammatory changes in the afferent nerves from the aortic arch and carotid sinus. *J. R. Bignall*

2997. **Familial Neurofibromatosis with Multiple Cranial Lacunae.** (Neurofibromatose familiale avec lacunes craniennes multiples)
—. GILBERT-DREYFUS, H. MAMOU, and R. WEISSENBACH. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **65**, 806–812, 1949.

See also Section Pathology, Abstract 2779.

Psychiatry

2998. **Psychiatric Observations on the Blind.** (Psychiatrische Beobachtungen an Blinden)
H. J. MEYER. *Nervenarzt* [*Nervenarzt*] **20**, 199–202, April, 1949. 4 refs.

Some of the possible relations between blindness and psychiatric illness are indicated and illustrated by 6 case histories. There is no specific disease picture. The appearances may be those of a reaction to entoptic hallucinations which are often of an alarming character or of an abnormal reaction to blindness, either depressive following the experience of blinding, or a paranoid reaction for which the ground has been prepared by the state of blindness. In both cases the previous personality may be " normal ", and in the latter differential diagnosis from an endogenous paranoid psychosis may be difficult. Blindness and endogenous psychosis may appear without connexion, or blindness and psychosis may result from the same organic brain disease. *W. Forster*

2999. **Observations of Nitrite-induced Postural Syncope in Patients with Mental Disease**
M. D. ALTSCHULE and M. LORENZ. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **71**, 6–9, May, 1949. 4 figs., 3 refs.

At the McLean Hospital, Waverley, Mass., and the Harvard Medical School, the authors studied the reactivity of postural vasoconstriction mechanisms in 24 normal subjects and 20 patients suffering from mental diseases and psychoneuroses including schizophrenia (11), chronic alcoholism (3), paranoia, mania, anxiety neurosis, reactive depression and other non-schizophrenic conditions. Sodium nitrite, 3 gr. (0·2 g.), was given orally 3 to 4 hours after a meal. After 30 minutes' rest the subject lay on a board at right angles to which was fixed a bicycle seat which he straddled. After control observations, the subject's head was then raised, the board being tilted 60 degrees, and the systolic pressure was recorded every few minutes. If syncope did not occur within 40 minutes the test was stopped and repeated not less than 2 days later with 7 gr. (0·45 g.) of nitrite. In the control subjects syncope occurred after the larger or smaller dose of nitrite, indicating normal vasomotor reactivity. Of the 11 schizophrenic patients syncope occurred in 4, but a fall or rise in blood pressure without syncope, indicating a definite increase in vasomotor reactivity, occurred in the other 7 cases after taking 7 gr. of nitrite. Of 7 schizophrenics tested 4 months or more after lobotomy 4 showed definite or marked increases in vasomotor reactivity, but no consistent change in reactivity had taken place in 3 of these patients who had also been tested before operation. An increase in reactivity was found in 4 of the 9 patients with non-schizophrenic diseases.

Distressing visual hallucinations occurred a few minutes after the blood pressure began to fall in each of 11 tests on a patient with involutional psychosis. When he returned to the horizontal state the visions ceased and the patient became aware that these had been hallucinations. Another patient spoke freely for the first time of incidents in her past history which had previously been suppressed, and a manic patient became more excited when the blood pressure began to fall. The similarity of findings in schizophrenia and in non-schizophrenic cases does not suggest that the former is accompanied by a specific change in autonomic function, nor that the autonomic system is less responsive. The findings after lobotomy indicate that no distinctive change in postural vagomotor reactivity can be found as a result of the operation when time for complete healing is allowed.

G. de M. Rudolf

3000. **Birth Injury as a Cause of Mental Defect: The Statistical Problem**
L. S. PENROSE. *Journal of Mental Science* [*J. ment. Sci.*] **95**, 373–379, April, 1949. 1 fig., 16 refs.

There has been considerable difference of opinion as to how far birth injury may be responsible for mental defect. The general opinion has been that if the paresis associated with mental defect is asymmetrical the whole syndrome is more likely to be traumatic in origin than if the paresis is symmetrical. After reviewing the rather inconclusive literature the author analyses a series of 1,280 mentally defective patients investigated between 1930 and 1937. In his opinion only 11 (8 male and 3 female) showed physical signs which, combined with the history of a difficult labour, warranted the diagnosis of birth injury as the main cause of their mental defect. All but one of these showed signs of a pyramidal lesion, usually unilateral or, if bilateral, affecting the two sides unequally, and 7 were epileptic. In one case there was associated pituitary dysfunction. Some points of similarity were found with cases of mental defect due to postnatal injury. The series is too small to be of much significance but surprisingly little reliable work has been done on the subject. *R. G. Gordon*

3001. **Changes in Palmar Skin Resistance During the Rorschach Test. II. The Effect of Repetition with Color Removed.** [In English]
F. V. ROCKWELL, L. WELCH, J. KUBIS, and V. FISICHELLI. *Monatsschrift für Psychiatrie und Neurologie* [*Mschr. Psychiat. Neurol.*] **116**, 321–345, Dec., 1948. 1 fig., 2 refs.

In the Rorschach test it has been found that with some subjects, more unstable, tense, and emotionally labile than others, the introduction of colour induces an inhibition of verbal responses and of autonomic responses

as measured by a continuous graphic record of electrical resistance of palmar skin. In the present series 23 apparently normal female undergraduates were tested by the exhibition of coloured Rorschach cards and a week later by the exhibition of the same designs but without colour. Fifteen showed no evidence of colour shock; 8 showed definite colour shock. Verbal responses and autonomic resistance were recorded. On re-testing all subjects showed a significant increase in verbal responses to all cards. The increases were relatively greater in the case of the originally non-coloured cards than in the case of the originally coloured cards.

The removal of colour on re-testing was not followed by significant differences in verbal responses between the two groups of subjects, but in the group not showing colour shock there was a uniform increase in autonomic responsiveness. It was thought that this indicated a relative inability in the group showing colour shock to mobilize normal defence mechanisms, that this group was therefore more potentially psychoneurotic than the other, and that this test may be useful in detecting such persons. *R. G. Gordon*

3002. **The Metabolism of Glutamic Acid**
H. WAELSCH. *Lancet* [*Lancet*] **2**, 1–4, July 2, 1949. 21 refs.

3003. **A Case of Hystero-epilepsy Successfully Treated by Deep Analytic Psychotherapy**
H. EDELSTON. *Journal of Mental Science* [*J. ment. Sci.*] **95**, 388–402, April, 1949. 9 refs.

The author points out that in his admirable description of epilepsy and discussion of its causation, Hughlings Jackson made no mention of a possible psychological cause or of psychological treatment. On the other hand, Worster-Drought, in referring to Jackson's work, does make reference to these aspects and invokes the help of psychotherapy in the treatment of many cases. The author is convinced that deep analysis might do much good, even in cases apparently entirely organic in origin. A fairly detailed description is given of the analysis of a young man suffering from what seemed to be true organic epilepsy. The treatment was stormy and prolonged, but was eventually completely successful after a 6-year follow-up. Marked ambivalent feeling for the mother was the main feature of the findings, with strong narcissism and sibling jealousy. It is pointed out that the supposed epileptic personality resembles that of all sorts of psychoneurotic patients and out of this basis epileptic symptoms may develop in certain hysterical subjects. Further detailed and prolonged studies (250 sessions in this case) are needed to elucidate the subject.
R. G. Gordon

3004. **Sex-hormone Relationships in Schizophrenic Men**
R. G. HOSKINS and G. PINCUS. *Psychosomatic Medicine* [*Psychosom. Med.*] **11**, 102–109, March–April, 1949. 16 refs.

Difficulties in adjustment in the psychosexual field have been observed in schizophrenia, both before and after the onset of the psychosis. For this reason the steroid components in the urine were estimated in 21 schizophrenic men, 23 normal men, and 11 normal women. The urine samples were 48- to 72-hour collections; in most cases androgen, oestrone, oestriol, oestradiol, and 17-ketosteroids were estimated. In the group of schizophrenic patients, the total oestrogen output was lower than in the women but higher than in the men of the control group; the androgen output of the patients exceeded that of the women and fell below that of the men. The mean androgen–oestrogen ratio in the women was 2·3; in the men 16·3; and in the patients 9·7. In these respects the excretion of steroids in schizophrenic men showed a definite approach towards the feminine pattern.

The 5 patients with the lowest androgen/oestrogen ratio were weak-spirited and non-aggressive; homosexual trends were not marked. The 4 with the highest ratio were more highly sexed, more energetic, and more aggressive; three of the 4 showed more or less clear evidence of homosexuality. *Desmond O'Neill*

PSYCHOSOMATIC MEDICINE

3005. **Physiologic Mechanisms of Psychosomatic Phenomena**
S. WOLF, T. H. HOLMES, H. GOODELL, and H. G. WOLFF. *Pennsylvania Medical Journal* [*Penn. med. J.*] **52**, 681–688, April, 1949. 19 refs.

A method of study was agreed upon in which variations in disease, particularly in nasal disorders, were noted in connexion with events and with the life history. A résumé is given of attitudes and behaviour in 100 sufferers from rhinitis, from which the conclusion is drawn that deprivation of parental love and other frustrations caused a defensive mentality and terminated in a " shutting in and shutting out reaction " reflected in the nasal passages.

Experiments are described in which the nasal mucosa was irritated with fumes of ammonium carbonate, resulting in hyperaemia, lacrimation, and spasm of the eyelids. In another experiment severe headache was induced by fitting on a tight steel crown which constituted a non-specific threat not directed at the nasal passages; the sense of apprehension produced the same nasal hyperaemia as did the direct action of noxious fumes, and of pollen in a hay-fever patient. In order to ascertain whether emotional reaction would achieve the same result as physical trauma, a sufferer from chronic rhinitis was tested with stories of his wife's inimical attitude towards him; this caused nasal hyperfunction, obstruction to breathing, and extreme emotional disturbance. The conclusion of the investigators is that tears serve to wash away particles, and dilute noxious agents, and that the infantile behaviour pattern built around weeping may persist in adult males as hyperfunction of the nasal mucosa, under chronic mental stress. This tends to the growth of polypi and the establishment of the infection in the sinuses. The neural mechanism involved includes the parasympathetic branches of the third cranial nerve, the superficial petrosal nerve, and the sphenopalatine ganglion. Hyper-

function and hypofunction of organs under emotional stimuli have been noted especially in the case of the stomach, in which hypofunction occurs in connexion with the stimuli of fear, disgust, and dejection. In contrast, hyperfunction is more destructive of tissue, and is associated with tension, rage, and aggressive behaviour. The above findings are said to relate to the function of other organs, including bladder, colon, salivary glands, and vagina. *C. S. Nicholson*

3006. **Relation of Changes in Carbohydrate Metabolism to Psychotic States**
H. FREEMAN and R. N. ZABORENKE. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **61**, 569–576, May, 1949. 1 fig., 7 refs.

A study was made to discover possible effects of changes in the emotional state on the glucose-tolerance curve of 28 psychotics. The emotional changes were induced by electric shock therapy. On the whole the glucose-tolerance curve was little affected by the changes, remaining abnormal. *P. W. Nathan*

3007. **Pain Charts. A Description of a Technique Whereby Functional Pain may be Diagnosed from Organic Pain**
H. PALMER. *New Zealand Medical Journal* [*N.Z. med. J.*] **48**, 187–213, April, 1949. 26 figs.

This paper outlines a method for the recording of a patient's complaint of pain. The patient is given charts of the front and back of the body and invited to mark on them every pain which he feels. If he can distinguish different qualities of pain, the observer marks the site of each with ink of different colours. The patient may be asked which pain causes him the most concern.

Pain associated with functional nervous disorders is found as a rule to show a striking symmetry; such symmetry is almost diagnostic of a functional nervous disorder or of a functional superstructure built up round an organic lesion. Where the chart shows asymmetrical pain, there may be preoccupation with the heart and circulation, a history of operation or injury, introjection of another person's pain, a psychotic syndrome, an iatrogenic condition, an occupational neurosis, or a true psychalgia. The pain record of one patient is often reproduced very closely by another. The main sites of functional pain in each region of the body are described in detail. A number of pain charts from patients with various functional disorders are given.

[The value of this method in recording the patient's description of his pain is clear. The author's subtitle for his article, " A technique whereby functional pain may be diagnosed from organic pain ", implies, however, that description alone is sufficient for this purpose. The differential diagnosis surely rests on other aspects of the pain experience as well.] *Desmond O'Neill*

3008. **Some Interpersonal Factors in Illness**
F. R. C. CASSON. *Lancet* [*Lancet*] **2**, 681–684, Oct. 15, 1949. 5 refs.

See also Section Paediatrics, Abstract 2810.

TREATMENT

3009. **Treatment of Mental Illness at Home by Small Doses of Insulin. A Follow-up Report and Appraisal of Results in Twenty-six Cases**
N. COHEN. *New England Journal of Medicine* [*New Engl. J. Med.*] **240**, 669–676, April 28, 1949. 31 refs.

The author reviews a previously reported series of 12 cases, and the results in a further series of 14 new cases. The conditions treated include anxiety state (8 cases), depressive psychosis (7 cases), schizophrenic reaction (7 cases), emotional instability (2 cases), obsessive compulsive state (1 case), and manic-depressive psychosis (1 case). Seventeen of the patients were restored to their pre-morbid state by insulin sub-coma treatment, and were entirely free of any residual symptoms at periods ranging from 11 to 40 months after the periods of treatment. Premature interruption of treatment influenced the clinical result in 6 cases. Two patients relapsed, but improved later with electric convulsion therapy. Only in 2 patients was there relapse and regression.

The technique of the treatment involves very careful physical examination, including electrocardiography and chest radiography. Contraindications include metabolic disturbances, acute and chronic liver and kidney disease, active pulmonary tuberculosis, and myocardial damage. The possibility of hypersensitivity to insulin should not be overlooked, but it is of infrequent occurrence in the method used. Having fasted for from 4 to 12 hours, the patient is given insulin by deep intramuscular injection of 5 to 15 units. The dose is increased by about 10 units daily until mild hypoglycaemia (lassitude, perspiration, hunger, thirst, and somnolence) is produced. The dose is then kept at a minimum level but usually 50 to 100 units are sufficient to produce the desired reaction in about an hour. After 30 to 90 minutes the reaction is terminated by the administration of sugared fruit juice followed by a meal rich in carbohydrates. Quicker interruption of the hypoglycaemia is best carried out by the intravenous injection of 20 ml. of a sterile 33·3% glucose solution. Insulin treatment is carried out 6 days a week with one day's rest. Acute states require a shorter period of treatment than chronic ones. Patients should be observed for one month after the completion of therapy, which should be resumed at once in the case of a relapse. *D. S. Fairweather*

3010. **Electronarcosis at the Homewood Sanitarium, Guelph, Ontario**
J. J. GEOGHEGAN. *Journal of Mental Science* [*J. ment. Sci.*] **95**, 380–387, April, 1949. 11 refs.

The technique of electronarcosis is described, and the results of this method of treatment compared with those of insulin shock, both in cases previously untreated and in those in which electroconvulsive therapy had failed. Since electronarcosis is said to be more dangerous than insulin shock only physically fit patients were chosen, but on the whole electronarcosis appeared in practice to be the safer; so long as the electrodes are kept well

forward, currents of at least 150 mA can be used. The results suggest that the maximum benefit is obtained with 15 to 20 treatments, after which no further good is likely to accrue. Electronarcosis is not a specific form of treatment for schizophrenia, but the results so far obtained in recent cases were encouraging, although long-standing cases were not much affected. Mental disorders other than schizophrenia might well be treated by this method. It is concluded that, on the whole, electronarcosis is more effective than insulin shock, but patients in whom either method has failed should have the benefit of the other. *R. G. Gordon*

3011. **The Effect of Leucotomy on Creative Ability**
W. R. Ashby and M. Bassett. *Journal of Mental Science* [*J. ment. Sci.*] **95**, 418–430, April, 1949. 1 fig., 9 refs.

The authors devised a test to measure some aspects of creative ability, and applied it to 25 patients who had undergone leucotomy, a comparable group of 25 psychotic patients who had not been operated on, and 25 normal persons. Creative ability was defined as " that ability by which the ideational content of past experience is utilized in a situation to provide concepts and actions not directly evoked by the new situation, but elaborated by the patient's more complex cerebral reactions to the situation ". The test consisted of two parts. The subject was first asked to copy the colours of a simple picture. He was provided with a set of colours and a line drawing of the " example " picture. The task required little skill. In the second part of the test the " example " picture was removed and the subject instructed to paint another line drawing as he " would like to see it ". The difference between the second picture and the first was used as a measure of creative ability. The criteria used numbered 23, and the scoring was done independently by 2 observers, whose awards agreed in 89% of cases. The test was sufficiently specific and sensitive for measuring differences in the three groups of subjects. Both groups of patients had considerably less creative ability than the normal subjects, but there was no evidence that leucotomy tended to reduce creative ability. *F. K. Taylor*

3012. **The Results of Prefrontal Leucotomy in 68 Patients not Discharged from Hospital**
J. M. Rosie. *Journal of Mental Science* [*J. ment. Sci.*] **95**, 431–448, April, 1949. 19 refs.

The author reports on 68 patients at Crichton Royal, Dumfries, who had undergone prefrontal leucotomy but were still resident in a mental hospital 1 to 4 years after the operation. Of 60 patients with schizophrenia of long standing who had not responded to previous shock treatments, 39 improved after the operation, the greatest improvement occurring in catatonic and paranoid illnesses. Hallucinations and delusions disappeared in one-quarter of the schizophrenics, remained unchanged in another quarter, and were attenuated in the remainder; persistent aggression was lost and aggressive outbursts were reduced or modified. Three epileptic patients were operated on to combat psychic equivalents, slight success being achieved in 2 of them. Of 2 involutional melancholics, one was much improved and the other one unchanged. One manic-depressive patient was much improved; one patient suffering from post-encephalitic Parkinsonism remained unchanged; and one with general paresis who, after treatment with arsenicals, malaria therapy, and inductotherm therapy, retained grandiose delusions and vivid hallucinations, was slightly improved.

The most important frontal-lobe symptoms after the operation were euphoria, lesser elevation of mood, and inertia. Blunting of ethical and social feelings was observed in a few improved patients. The importance of post-operative care and re-education is emphasized. After the operation 46 of the patients required electric convulsion therapy transiently or as maintenance treatment. Regression occurred temporarily in 16 and permanently in 14 patients. Epileptiform fits occurred for the first time in 6 leucotomized patients. Increase in weight was the most striking vegetative manifestation of frontal-lobe deficiency; it was not associated with improvement. A prognostically favourable pre-operative sign was marked mental tension. The result of the operation cannot, however, be predicted in individual cases. Obsessional illness and affective psychoses respond best to leucotomy, as is shown by a comparison of the patients in this series with a group of patients discharged from the same hospital after leucotomy and reported by Frankl and Mayer-Gross (*Lancet*, 1947, **2**, 820). *F. K. Taylor*

3013. **Preliminary Report of Changes after Prefrontal Leucotomy**
A. Petre. *Journal of Mental Science* [*J. ment. Sci.*] **95**, 449–455, April, 1949. 13 refs.

The author examined 4 male and 16 female patients of St. George's Hospital, London, before and 2 to 3 months after leucotomy. The patients were " severe neurotics rather than psychotics " and able to co-operate during 5 to 6 hours of psychological testing. After the operation there was a significant drop in the Wechsler verbal intelligence quotient, mainly attributable to answers about social attitudes. The capacity for generalizations was reduced when measured by a test requiring the explanation of six proverbs. There were a loss of mental age on the Porteus maze test and an indication of decreased learning ability. " Neuroticism ", tested by Hull's " body sway suggestibility " test and the evenness of work curves, was found to be reduced. " Introversion " was considered less marked, because after operation patients became quicker though not so accurate, were less persistent and less self-reproachful, living less in the past and being more optimistic about the future. It was also found that after operation patients were less easily distracted by extraneous stimuli, and frequently misused common words or formed new ones. *F. K. Taylor*

3014. **Social Work and the Ex-serviceman: The Psychiatric Problem**
A. Stoller. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 639–646, May 14, 1949. 13 refs.

Infectious Diseases

3015. **A Five Day Peroral Treatment of Yaws with STB, a New Trivalent Arsenical**
E. A. H. FRIEDHEIM. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **29**, 185–188, March, 1949.

A drug for the mass treatment of yaws in the less developed parts of the tropics should be cheap, chemically stable, safe, easily administered, and effective in a short course of treatment; for these reasons the author commends the 3-weeks' course of injections of acetarsol and bismuth salicylate of the Sierra Leone Health Service, although effective oral treatment would be preferable. He has prepared a relatively non-toxic and stable tervalent derivative of acetarsol, named "STB", which is 4-oxy-3-acetylaminophenylarsenoxide. It was tested in 88 cases of yaws in the district of Gueckedou, French Guinea, 73 of these being of the infectious type and 15 non-infectious (crab yaws); each patient was given by mouth a daily dose of 0·01 to 0·02 g. per kg. body weight for 5 days. Exudative lesions were epithelized by the fifth day, crevices and fissures had healed, and the soles of the feet had become painless and non-sensitive in many cases; 3 months after treatment 87 patients out of 88 were cured. Similar results were obtained in 75 cases of yaws in the Belgian Congo; all the patients except one were clinically cured one month after treatment, and after 5 months 69 were still clinically cured while 5 had relapsed. The drug caused no untoward effects.

J. F. Corson

3016. **Miracil. Clinical Trial on Patients Infected with *Schistosoma haematobium* and *S. mansoni***
D. M. BLAIR, F. HAWKING, C. V. MEESER, and W. F. ROSS. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **4**, 68–80, March, 1949. 13 refs.

"Miracil D" is the hydrochloride of 1-methyl-4-β-diethylaminoethylaminothioxanthone. It was synthesized originally by Mauss and shown to have considerable therapeutic activity in mice and monkeys infected with *Schistosoma mansoni* (Kikuth *et al.*, *Ann. trop. Med. Parasit.*, 1948, **42**, 256). Miracil is rapidly absorbed from the alimentary canal, but only about 7% of the drug is excreted in the urine and little appears in the faeces. There is little tendency for accumulation, so the major portion must be degraded in the body.

The authors have carried out a clinical trial of this drug in patients infected with *S. haematobium* and *S. mansoni* at Salisbury, Southern Rhodesia. After treatment the patients (mostly children) were followed up at 7-day intervals for at least 16 weeks, urine and stools examined, and the patient classified according to whether (1) active miracidia could be hatched; (2) living eggs were found but no miracidia hatched; (3) only dead eggs were present; or (4) no eggs could be detected. The findings were only regarded as "negative" if there were no eggs, or if only calcified eggs were present. Of 40 patients infected with *S. haematobium* and treated with daily doses of 4 mg. per kg. body weight for 3 weeks (total dose 80 to 100 mg. per kg.) 11 were free from infection 12 weeks later. Included in this series were 11 cases of concurrent *S. mansoni* infections—only 1 of which became negative. Treatment of 13 boys with 0·6 g. daily for 15 days to a total of 35 to 150 mg. per kg. resulted in the findings in 10 of them becoming negative 3 weeks after completion of treatment. Daily doses of 10 mg. per kg. for 10 days to a total dosage of 90 to 100 mg. per kg. in 18 children infected with *S. haematobium* resulted in negative findings in 14 of them 6 weeks after treatment. The drug was well tolerated, occasional side reactions being observed, consisting of abdominal pain, nausea, and vomiting. In patients taking about 3 mg. per kg. daily the blood concentration 2½ hours after the dose was 0·3 to 0·8 mg. per 100 ml. It is suggested that the daily therapeutic dose should be at least 10 mg. per kg.

R. Wien

VIRUS INFECTIONS

3017. **Experimental Studies on Rabies Virus**
H. KOPROWSKI. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **40**, 60–67, Feb., 1949. 6 refs.

The Flury strain of rabies virus was grown in developing chick embryos for the manufacture of a vaccine which was used to immunize guinea-pigs and dogs. When these animals were injected later with virulent virus they were shown to possess a degree of resistance lacking in controls. An antiserum obtained from rabbits was used to prevent the development of the disease in hamsters which had been inoculated with virulent rabies virus. This antiserum was found to be of value if given within 24 hours of the inoculation, and administration was much more effective than injection of commoner rabies vaccines, which were found to be of little or no value in these animals.

Scott Thomson

3018. **Treatment of Herpes Zoster with Moccasin Venom**
C. C. DENNIE, D. B. MORGAN, and F. P. COOMBS. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **12**, 153–155, March, 1949. 4 refs.

Twenty patients—14 males and 6 females ranging in age from 22 to 87—with herpes zoster were treated with moccasin venom. Most had had signs and symptoms for from 3 to 8 days. Almost all the spinal nerves and the fifth cranial nerve were involved. Moccasin venom 1 in 3,000 was given intradermally, the initial dose being 0·1 ml. The dose was maintained at this level in 6 cases, not more than three injections being given. The rest received not more than 0·3 ml. per dose, generally

0·15 ml. for the second and 0·2 ml. for the third and last injection. The interval between doses was 2 or 4 days. Of the 20 patients, 18 were improved and 4 recovered dramatically, being free from pain and completely cured within 4 days. Corneal involvement was rapidly checked in 2 cases and was probably prevented in 2 others. Reactions were usually local and insignificant. The authors consider this is the best remedy for herpes zoster they have yet encountered, and that it is of special value in cases with corneal involvement.

James Marshall

3019. **Potential Vectors of Japanese Encephalitis in the Caroline Islands**

H. S. HURLBUT and J. I. THOMAS. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **29**, 215–217, March, 1949. 6 refs.

Although Japanese encephalitis is not known to occur on Ponape in the Eastern Caroline Islands, it has been found on Guam and may spread to other tropical islands of the Pacific. The authors have tested the possibility that the mosquitoes *Culex quinquefasciatus* Say and *C. annulirostris* Skuse, both obtained from Ponape, may be potential vectors of the virus. Both these mosquitoes are nocturnal in their habits, feed readily on man, and are common about human dwellings in many parts of the Pacific. The insects were reared in the laboratory and fed on infected mouse brain. After an extrinsic incubation period of 6 to 8 days at 30° C. the mosquitoes were permitted to bite suckling mice 4 to 7 days old. Reeves and Hammon (*J. exp. Med.* 1946, **63**, 185) have previously shown that *C. quinquefasciatus* can transmit Japanese encephalitis to mice. The present authors have confirmed these findings and also obtained positive results with *C. annulirostris*. *F. O. MacCallum*

3020. **Report on the Presence of Japanese B Encephalitis Neutralizing Antibody Among Filipinos and Certain Philippine Animals**

E. S. SALAFRANCA and L. ESPIRITU. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **29**, 219–227, March, 1949. 8 refs.

Owing to the heavy interchange of military personnel between the Japanese islands and the Philippine Islands, it was considered advisable to make a survey of Japanese B encephalitis in the Philippines, neutralization tests in mice and complement-fixation tests being used. Specimens of serum from 3 small groups of persons and 4 of animals of different species were tested. Of 21 specimens from normal adult Filipinos, 7 gave positive results on neutralization test, as did 14 of 17 from Japanese prisoners of war. Also, in 5 of 13 cases of suspected encephalitis in humans, an increase in neutralizing antibodies was found in the blood. As the disease is unknown in the Philippines, it is difficult to explain the rise in titre unless other unknown viruses will stimulate such reactions. The serum of carabaos, horses, goats, and cattle all had a content of neutralizing antibodies so high that the authors consider it unlikely that the reaction was non-specific. *F. O. MacCallum*

3021. **The Epidemiology of Primary Herpes Simplex Infection**

S. G. ANDERSON and J. HAMILTON. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 308–311, March 5, 1949. 2 figs., 6 refs.

In 1938 Dodd, Johnson, and Buddingh showed that herpes simplex virus could be isolated from most cases of aphthous stomatitis of infants, and in 1939 Burnet, Lush, and Williams proved by finding rising antibody titres that this disease was the primary herpetic infection of these infants. [The greater events of the second world war seem to have largely obscured this discovery so far as British textbooks are concerned. Now an important addition to this knowledge comes from Burnet's co-workers in Melbourne.]

The present authors studied the incidence of stomatitis among 240 infants and young children over a period of 11 months in a Melbourne orphanage. Of these children, 51 had had no previous history of stomatitis or of herpes febrilis, and these were bled at intervals of 4 months throughout the year and their sera examined for herpes antibody. Twenty of the 51 children had an attack of stomatitis during the year, and 2 of these a recurrence. In 3 out of 4 trials among these cases herpes virus was isolated by inoculation of mouth swabbings into the scarified cornea of a rabbit. None of the 20 children had herpes antibody in the serum before the attack of stomatitis, but after this episode the level of antibody in the serum of all was comparable with that in adults subject to labial herpes. This is in agreement with the concept previously established for the relation between primary herpetic stomatitis and the secondary labial herpes so common in adults.

The most interesting observations, however, were made on the 31 children without clinical evidence of stomatitis, although they must have been exposed to the infecting virus on many occasions. These were divided into 4 groups. (1) Ten infants, of ages 3 to 15 months, who at the time of the first bleeding had a significant antibody level. In all these cases the titre progressively decreased to reach a negligible level. This group was considered to have gradually diminishing maternal immunity. (2) Nine children with no antibody in the first sample of serum, but in whom between the ages of 11 and 20 months a high level of antibody developed in the absence of clinical evidence of herpetic infection. This group was considered to have become immune by subclinical infection. (3) Seven children, all over 17 months of age at the beginning of the survey, who had a high antibody titre throughout. This group must already have become immune by subclinical infection. (4) Six children, varying in age from 15 to 19 months, who had never had any antibody in their blood during the period of the survey. Two of these, however, were found to have developed antibody 3 months later. This group therefore was considered to be one in which maternal immunity persisted for a time after detectable antibody had disappeared from the blood. This conclusion was also based on the probability that the mothers of these infants suffered from herpes, since it has been shown that herpetic infection is predominantly a disease of the

poorer classes. This study suggests that between the ages of 7 and 14 months in most children maternal antibody can no longer be detected, although they are still immune to the infection; that the age of primary herpetic infection in a heavily infected environment is between 11 and 22 months, with the majority infected at 14 months; and that nearly half of the children heavily exposed to infection have subclinical infections. The authors raise the question whether vaccination with killed herpes virus about the age of one year, repeated later if necessary, might protect against herpetic infection until the child had reached the age of non-immunological resistance which they consider to be characteristic of adult tissues. *H. Stanley Banks*

POLIOMYELITIS

3022. **The Incidence of Poliomyelitis in Cases of Mild Illness During a Severe Urban Epidemic**
G. C. BROWN, J. D. AINSLIE, and T. FRANCIS. *American Journal of Hygiene* [*Amer. J. Hyg.*] **49**, 194–199, March, 1949. 12 refs.

Poliomyelitis virus was recovered from the stools of 7 out of 20 patients (mostly children) examined at a general hospital in Minneapolis during the summer of 1946, but sent home because, in the view of the examining officers, the diagnosis of poliomyelitis could not be confirmed. The diagnoses made at the hospital on these " rejects " included pharyngitis, upper respiratory infection, and gastro-intestinal infection. The correct diagnosis in many of these cases was evidently the " minor illness " of poliomyelitis. The virus was also recovered from the stools of 7 out of 23 patients with similar illnesses seen in their homes by visiting nurses, and from the stools of 2 out of 22 persons who had remained well during the month preceding the collection of specimens and who had had no known association with diagnosed cases of poliomyelitis. In many of the cases in which virus was isolated, the specimens were not collected until 5 to 6 weeks after the onset of illness. This raises the question whether the presence of virus represents persistence of infection or is unrelated to the illness. *A. J. Rhodes*

3023. **Carditis in Poliomyelitis. An Anatomic Study of Thirty-five Cases and Review of the Literature**
T. E. LUDDEN and J. E. EDWARDS. *American Journal of Pathology* [*Amer. J. Path.*] **25**, 357–381, May, 1949. 20 figs., 24 refs.

In 35 fatal cases of poliomyelitis examined post mortem at the Mayo Clinic the heart weight was found to be increased, the right ventricle was dilated, and there was oedema and thickening of collagen fibres in the mitral and aortic valves. In one case organizing fibrinous vegetations were found on the mitral valve. In 14 of the 35 cases there were microscopic foci of myocarditis affecting particularly the interventricular septum and the left posterior papillary muscle. The muscle fibres showed areas of degeneration or necrosis, associated in one instance with perforation of the interatrial septum. There were interstitial congestion and oedema, and infiltration with polymorphonuclear leucocytes, lymphocytes, plasma cells, and monocytes.

Carditis is difficult to recognize clinically in poliomyelitis, and in these cases the diagnosis was made on microscopical examination only. It was commoner and more severe in adults than in children and was not related to the severity of the attack. Rheumatic fever and the administration of serum and sulphonamides were not thought to have played any part in aetiology in this series. While anoxia and toxaemia may well be important in this respect, it is considered that a direct action of the poliomyelitis virus on the myocardium cannot be excluded. *R. C. B. Pugh*

3024. **Paralytic Poliomyelitis. The Early Symptoms and the Effect of Physical Activity on the Course of the Disease**
W. R. RUSSELL. *British Medical Journal* [*Brit. med. J.*] **1**, 465–471, March 19, 1949. 12 refs.

The higher incidence of poliomyelitis among older patients in recent epidemics has made it easier to obtain reliable accounts from convalescents of the early stages of the illness and to assess the effects of physical activity upon its course. Of 100 collected cases of paralytic poliomyelitis analysed by the author, the onset in 85 occurred in Great Britain and in 83 of these during the 1947 epidemic—mainly in its latter half. Of the whole series 54 of the patients were adults and only 8 under 11 years of age. Few cases of purely bulbar disease are included; these patients either were unfit for questioning or had left hospital.

Typically, poliomyelitis has prodromal, pre-paralytic, and paralytic stages, but the attack may abort in the first or second of these. Diagnosis of attacks confined to the prodromal stage must usually be conjectural, but a typical pre-paralytic stage can often be diagnosed correctly, even if no paralysis follows. Occasionally, too, the prodromata include spinal symptoms suggestive of the early presence of the virus in the spinal cord. In 34 of 84 typical paralytic cases a history of a prodromal illness was obtained and this preceded the spinal symptoms of the pre-paralytic stage by 5 days on the average. The pre-paralytic stage is the critical period of the illness, but it is emphasized that neither its severity nor the degree of change in the cerebrospinal fluid gives any indication of the severity of the ensuing paralysis. Among the manifestations of the pre-paralytic stage headache (45%), compared with spinal pains and paraesthesiae (95%), was relatively insignificant and far less characteristic. It is noted that spinal rigidity without severe headache is unlikely to occur in meningitis. Spinal pains begin abruptly, are often localized, and may have a segmental distribution. The site of the pain often corresponds with the site of ultimate paralysis. Pre-paralytic pains and paraesthesiae affecting the chest, abdomen, and thighs may present diagnostic difficulties. Vertigo, jerking movements of the eyes, and vomiting may occur during the pre-paralytic stage, as may also nasal discharge, sore throat, diarrhoea, or constipation, but these last are not diagnostic. [Nasal discharge and

sore throat, however, among school-children during prevalence of poliomyelitis should be regarded with the utmost suspicion.]

In the pre-paralytic stage of " typical " cases spinal symptoms become increasingly severe for 2 or 3 days before paralysis appears and then subside, but occasionally these symptoms seem to be abating at the time paralysis develops, or paralysis may occur after the fever of the pre-paralytic stage has subsided. Again, the pre-paralytic stage may consist of two or more phases separated by intervals of comparative well-being. Paralysis may also spread in two phases. There were 11 " atypical " cases in the series of 100 : prodromata might merge into the spinal symptoms without the usual interval; the spinal symptoms might at first be vague, so making the day of onset uncertain, or they might be continued so long before paralysis developed as to alter the pattern of the disease. The battle with the virus reaches its climax during the pre-paralytic stage; the amount of spinal cord damage is then determined although it is possible that damage may sometimes occur during the prodromal stage. Convincing evidence is presented of the unfortunate effects of even moderate physical activity upon the course of the disease. The possible effects of activity before the pre-paralytic stage must be distinguished from the effects of activity during that stage. Local trauma may apparently determine the site of maximum paralysis, just as tonsillectomy increases liability to bulbar palsy. The author stresses the conclusion that " *complete physical quiet from the onset of symptoms will seldom fail to prevent serious paralysis, while strenuous or even moderate activity at this stage is highly dangerous* ". Therefore, knowledge of the ways in which the disease may present is essential for those having charge of aggregations of children. The season for poliomyelitis and for sports meetings should not coincide; during an epidemic physical activity should not be exhausting, and during minor illnesses should be avoided. The " working off " of symptoms by exercise is a perilous proceeding. In treatment, mental and physical quiet are essential. Rest for the muscles of respiration is especially important on both physical and psychological grounds. Respiratory weakness, of which weakness of coughing is an early sign, may be relieved by an artificial respirator, or, in mild cases, by the " lung inflator ", which is less worrying to the patient (*vide Lancet*, 1939, **1**, 206).

[This detailed critical analysis will repay close study.]

E. H. R. Harries

3025. **Poliomyelitis Virus of Low Virulence in Patients with Epidemic " Summer Grippe or Sore Throat "**
A. B. Sabin and A. J. Steigman. *American Journal of Hygiene* [*Amer. J. Hyg.*] **49**, 176–193, March, 1949. 2 figs., 13 refs.

It is estimated that in Cincinnati, Ohio, at least 10,000 cases of " summer sore throat " or " summer grippe " occurred during the late summer of 1947 in children aged 1 to 10. The onset was sudden with fever, headache, nausea or vomiting, vague epigastric distress or abdominal pain, sore throat, and generalized aching or soreness in certain muscles or joints. There was seldom any evidence of laryngo-tracheo-bronchial irritation. This epidemic was at its peak by the end of August, at which time few cases diagnosed as poliomyelitis were reported; however, the number of such cases increased later and reached a total for the year of 170, the highest since 1936. Detailed clinical and virus studies were carried out in 10 cases of the former disease. Of these patients only 2 developed transitory nuchal or spinal rigidity associated with pleocytosis of the cerebrospinal fluid, warranting a clinical diagnosis of non-paralytic poliomyelitis. Poliomyelitis virus of high virulence for monkeys was recovered from throat swabs and stools of one of these patients, and the other developed antibodies for the Lansing strain in convalescence. Among the 8 patients without nuchal or spinal rigidity, 3 had cerebrospinal pleocytosis. Poliomyelitis virus of very low virulence for monkeys was present in the stools of 2 of these 3 patients. Among the 5 remaining patients without rigidity or pleocytosis, poliomyelitis virus of low virulence was found in the throat swabs and stools of 2. The strains of virus recovered from clinically diagnosed cases of poliomyelitis occurring during the same period were in each instance of high virulence for monkeys.

The impression was formed that there were in circulation in Cincinnati at the same time strains of poliomyelitis virus of high virulence for monkeys, associated with clinically recognizable cases of poliomyelitis, and strains of low virulence associated with the mild febrile illness diagnosed as " summer grippe ". *A. J. Rhodes*

3026. **Differentiation of Types of Poliomyelitis Viruses· I. Reinfection Experiments in Monkeys (Second Attacks)**
D. Bodian. *American Journal of Hygiene* [*Amer. J. Hyg.*] **49**, 200–224, March, 1949. 4 figs., 31 refs.

This paper is concerned with the important problem of the occurrence of second attacks of poliomyelitis, with particular reference to the disease in monkeys. It is plain that conclusive evidence that two attacks of poliomyelitis have occurred in the same animal is difficult to obtain, as virus isolation from the central nervous system is not practicable at the time of the first attack. However, the typical clinical picture, with severe paralysis, appearing in reinoculated monkeys at the time when controls are affected, provides very convincing evidence. For this purpose, the following diagnostic criteria must be satisfied. In the first attack: (1) Definite paralysis, usually preceded by fever, spasticity, and tremor. (2) The onset of atrophy in paralysed muscles after about 2 weeks. (3) The persistence of atrophy in at least one extremity. (4) The presence of lesions corresponding in age to the time of the first attack, with final confirmation of their nature by histopathological examination. And in the second attack: (1) Paralysis. (2) Recent lesions as determined histologically. The presence of Wallerian degeneration of the anterior roots, with a marked increase in nuclei, points to an attack 3 to 4 weeks earlier. (3) Isolation of virus from the cord.

Using the above criteria in re-infection experiments on monkeys, the author obtained the following important results: (1) Second attacks could not be produced with

homologous virus, even when doses as large as 10,000 PD 50 were given intracerebrally. Complete failure also resulted when viruses belonging to the same immunological type were used. This effect was reciprocal. (2) Second attacks were readily produced by inoculation with viruses apparently of a different type, the Lansing virus representing one type, and the Brunhilde, Kotter, and Frederick viruses the other. However, the second-attack rate with heterotypic inoculation was always significantly less than the normal-control attack rate, so that obviously some monkeys were protected against the heterotypic virus. (3) The second-attack rate was not significantly different in groups of animals in which the interval between the 2 inoculations varied between 1 and 5 months. If the second inoculation was made during the first 2 weeks of the disease, however, second attacks were unusual. (4) The second-attack rate was clearly lower in groups of animals which had been severely paralysed in the first attack than in those animals which had had a relatively mild first attack. (5) Second attacks were much less severe than the attack produced by the same virus in normal controls. The reduction in the severity was proportional to the severity of the first attack.

If these findings are applicable to the human disease one may conclude that second attacks are probably the result of exposure to a strain immunologically distinct from that which produced the first infection.

A. J. Rhodes

3027. **Differentiation of Types of Poliomyelitis Viruses. II. By Reciprocal Vaccination-immunity Experiments**

I. M. MORGAN. *American Journal of Hygiene* [*Amer. J. Hyg.*] **49**, 225–233, March, 1949. 6 refs.

This paper describes a method of typing strains of poliomyelitis virus based on cross immunity tests in vaccinated monkeys. Vaccination was carried out by the injection of live virus, in the form of a 20% suspension of the cervical and lumbar enlargements of the spinal cord of infected monkeys, into the calf or thigh muscles. Challenge doses were given by intrathalamic inoculation.

A series of 21 animals were vaccinated with various doses of Lansing virus, 4 of them developing paralysis after the first dose. All but one of the remaining 17 survived an intracerebral challenge dose of Lansing virus, and neutralizing antibody was shown to have developed in the serum. The immune monkeys were then given a " booster " dose of vaccine and were divided into 2 groups for challenge a week later by the nasal route, one group receiving Lansing and the other Brunhilde virus. Challenge of vaccinated animals by the nasal route obviates the risk that the injected virus may be partly neutralized by antibody at the site of inoculation. All in the latter group became paralysed, but none in the former. This surviving group, after another " booster " dose of vaccine, were then challenged nasally with Kotter virus; 4 of the 8 became paralysed, and histological evidence of poliomyelitis was found in the spinal cord of 2 of the others. A similar experiment showed that Lansing-immune monkeys became paralysed when inoculated intracerebrally with the Frederick virus.

Reciprocal tests were then performed. As vaccination by the intramuscular injection of virus of strains other than Lansing caused paralysis in a high proportion of cases, the vaccines had to be given by the subcutaneous route initially. Monkeys in the groups vaccinated with, and proved immune to, Brunhilde, Kotter, and Frederick strains were immune to the intracerebral injection of any of these 3 strains. In contrast, practically all of those vaccinated with, and immune to, Lansing virus succumbed to injections of the other 3. Clearly, therefore [and in confirmation of Bodian's results—see Abstract 3026] the 4 strains tested fall into two groups, one consisting of the Lansing virus, and the other consisting of the remaining three. Histological studies suggested that the immunity induced by vaccination not only prevents paralysis, but actually prevents infection of the central nervous system when the latter is directly exposed to virus.

A. J. Rhodes

3028. **Differentiation of Types of Poliomyelitis Viruses. III. The Grouping of Fourteen Strains into Three Basic Immunological Types**

D. BODIAN, I. M. MORGAN, and H. A. HOWE. *American Journal of Hygiene* [*Amer. J. Hyg.*] **49**, 234–245, March, 1949. 18 refs.

By means of the methods previously described [see Abstracts 3026 and 3027], 14 strains of poliomyelitis virus have been investigated with a view to placing them in immunological types. Monkeys were vaccinated with the Lansing or Brunhilde " prototype " strains, challenged with homologous virus cerebrally, given a " booster " dose of vaccine, and one week later challenged with the unknown virus. Vaccinated monkeys surviving challenge with both the vaccinating and one test virus were given another " booster " and challenged with another test virus. In this way, the strains of virus tested were grouped into three basic immunological types as follows:

Brunhilde Group	*Lansing Group*	*Leon Group*
Brunhilde	MEF 1	Leon
Frederick	MV	
Kotter	Wallingford	
Riley		
MEF 2		
Minn.		
Sudeck		
Per		
Beich		

The Leon strain (isolated in Los Angeles in 1937 by Kessel) appears to be unrelated to the other viruses studied. The interesting observation is made that 3 characteristic clinical attacks of poliomyelitis at intervals of about 2 months occurred in 2 monkeys inoculated successively with Wallingford, Leon, and Brunhilde viruses. It is also pointed out that only those strains known to be related to the Lansing strain have been passaged in rodents.

[This series of three papers constitutes one of the main contributions to poliomyelitis in recent years. The question of the antigenic structure of the prevalent types of virus is of fundamental importance to our fuller

understanding of the epidemiology and immunology of this disease, and has a bearing on the possibility of elaborating a virus vaccine.] *A. J. Rhodes*

RICKETTSIAL INFECTIONS

3029. **Q Fever Studies in Southern California. III. Effects of Pasteurization on Survival of *C. burneti* in Naturally Infected Milk**

R. J. Huebner, W. L. Jellison, M. D. Beck, and F. P. Wilcox. *Public Health Reports, Washington* [*Publ. Hlth Rep., Wash.*] **64**, 499–511, April 22, 1949. 5 refs.

Controlled tests of the efficiency of the holding-vat and the " high temperature short time " (H.T.S.T.) techniques of pasteurization were carried out on milk known to contain sufficient *Rickettsia burnetii* readily to infect guinea-pigs. Mice and guinea-pigs were inoculated intraperitoneally with the milk under test, and a positive complement-fixation reaction for Q fever 30 days after the injection was taken to indicate the presence of infection. Of 52 guinea-pigs injected with raw milk 48 gave positive complement-fixation reactions. No evidence of infection was found in 36 guinea-pigs injected with H.T.S.T.-pasteurized milk, whereas 3 of 48 injected with vat-pasteurized milk gave positive reactions. Similar results were obtained in mice. Thirty-two bottles of vat-pasteurized whole milk and 4 bottles of vat-pasteurized cream obtained from Los Angeles markets were injected into guinea-pigs. Three specimens of whole milk and one of cream gave positive serological evidence of Q fever. The possible importance of milk as a reservoir of Q-fever infection is mentioned. The resistance of *R. burnetii* to heat and the results of these experiments suggest that the holding-vat method of pasteurization cannot be relied on to eradicate such infection from milk. *J. L. Markson*

3030. **Histopathologic Observations in a Fatal Case of Q Fever**

T. L. Perrin. *Archives of Pathology* [*Arch. Path.*] **67**, 361–365, April, 1949. 3 figs., 8 refs.

In this paper are described the histological findings in a previously recorded case. A 43-year-old cattle-worker died after a 15-day illness characterized by fever, cough, nasal congestion, headaches, and mental confusion. On inoculation of guinea-pigs with blood drawn 3 hours after death and with post-mortem sternal marrow a positive response was obtained to complement-fixation tests for Q-fever virus and rickettsiae were demonstrated in smears. It should be mentioned that necropsy was performed 40 hours after death on a body embalmed by arterial injection only. Necropsy revealed a diffuse consolidation of lungs, microscopy showing an essentially mononuclear exudate, with congestion and haemorrhages, but neutrophil granulocytes were not infrequent and there was a fibrin network. No rickettsiae or other micro-organisms could be found. Focal hypoplasia was seen in the sternal marrow. In the myocardium there was fairly extensive ischaemic fibrosis due to occlusion of a major coronary vessel. No significant change was found in other organs. It is concluded that the lung changes were essentially due to the Q-fever virus, and possibly also the marrow hypoplasia; however, the cardiac condition certainly seems to have had an unfavourable influence in a disease usually benign in the healthy adult. *W. S. Killpack*

3031. **Clinical Aspects of Q Fever in Southern California: A Study of 80 Hospitalized Cases**

R. B. Denlinger. *Annals of Internal Medicine* [*Ann. intern. Med.*] **30**, 510–527, March, 1949. 4 figs., 8 refs.

Epidemics of Q fever are reported from time to time in Southern California, Texas, and Illinois. The malady is an acute specific fever marked clinically by chilliness, headache, general malaise, cough, anorexia, and pleuritic pain. Meningism, prostration, and bradycardia are occasional features. Common elements in severe cases are " atypical pneumonia " and various forms of acute pleurisy and pulmonary infiltration. The infection is caused by *Rickettsia burnetii* following exposure to cattle or agricultural material or the drinking of unpasteurized milk. Diagnosis is established by specific complement-fixation tests, and the disease is treated by aureomycin. *G. F. Walker*

3032. **Destruction of Nerve Cells by Rickettsial Organisms of Tsutsugamushi Fever**

J. W. Papez and J. F. Bateman. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **61**, 545–557, May, 1949. 14 figs., 13 refs.

See also Section Pharmacology and Therapeutics, Abstract 2719.

BACTERIAL INFECTIONS

3033. **Friedländer's Bacillus Meningitis Treated with Streptomycin**

J. F. Sadusk, A. S. Relman, R. R. Wagner, and R. Barnett. *American Journal of Medicine* [*Amer. J. Med.*] **6**, 522–529, April, 1949. 1 fig., 15 refs.

A case of meningitis with bacteriaemia due to Friedländer's bacillus (type B) was treated at first with sulphadiazine, and then with streptomycin 0·5 g. intramuscularly every 4 hours and 50 mg. intrathecally daily. Thirty-six hours later the temperature was normal and the clinical condition better. The cerebrospinal fluid and the blood became sterile and remained so. The patient died, however, on the sixth day. At necropsy a large abscess was found in the liver, in the pus from which Friedländer's bacillus was isolated. There was a large, flat, pink adherent mural thrombus in the hepatic vein. The gall-bladder wall was thickened. The right kidney weighed 305 g., and there were small scars in the pyramids, diffuse interstitial oedema, and necrosis of tubular epithelium. The left kidney weighed 135 g., the upper two-thirds being fibrotic with marked hyperplastic arteriosclerosis and endarteritis, together with oedema and round-cell infiltration of the submucosa of the pelvis. There was no obvious explanation for the sudden death following clinical improvement.

The authors note that 54 cases of meningitis due to Friedländer's bacillus have been reported. Before the advent of chemotherapy only one patient had been known to recover, but since then 4 more patients treated with sulphonamides or streptomycin have recovered.

R. Hare

3034. **Chloromycetin in Typhoid Fever**
W. H. BRADLEY. *Lancet* [*Lancet*] **1**, 869, May 21, 1949. 3 refs.

This is a preliminary announcement of a trial of chloramphenicol in typhoid fever, other investigations being still in progress. Some 37 persons from the village of Crowthorne, Berkshire, developed typhoid fever as a result of consuming an aliment infected with *Salmonella typhi*. The diagnosis was confirmed bacteriologically in all cases. The drug available was applied to the treatment of 6 out of 13 cases at the Victoria Infectious Diseases Hospital, Winchester, and 4 out of 9 cases at the South Middlesex Infectious Diseases Hospital, Mogden. In 9 treated patients (one very elderly patient died in the treated group, and one in a control group) signs of resolution were obvious within 48 hours after the administration of 8 g. of the drug. Seven patients were apyrexial by the third day, and the other 2 had normal temperatures on the fourth and fifth days. In the untreated patients the disease continued to run its usual course. There was every reason to believe that the initial encouraging results obtained by the use of chloramphenicol in typhoid fever will be confirmed. *R. Wien*

3035. **Treatment of Abortus Fever with Sulphonamides and Blood Transfusion**
C. ROMER. *British Medical Journal* [*Brit. med. J.*] **1**, 1035–1036, June 11, 1949. 2 figs., 2 refs.

See also Section Pharmacology and Therapeutics, Abstract 2719.

TUBERCULOSIS

3036. **Studies on the Chemotherapy of Tuberculosis.** [In English]
S. HASEGAWA. *Japanese Journal of Experimental Medicine* [*Jap. J. exp. Med.*] **20**, 69–101, March, 1949. 15 figs.

While in the West the chemotherapy of tuberculosis has relied on sulphones and antibiotics, Japanese workers have been experimenting with an alkaloid, cepharanthin ($C_{37}H_{38}O_6N_2$), derived from the roots and stem of *Stephania cepharantha* and *S. sasakii*. Both plants are members of the family Menisperaceae. Cepharanthin has been tested in human tuberculosis with very promising results. Of 37 patients in the first stage of pulmonary infection (Turban–Gerhardt classification) 32 were cured; among 24 second-stage patients 12 recovered; and among 229 in the third stage, 93. Patients with cavity formation were not so amenable to treatment as those with less pronounced lesions. The effects on lupus were striking when as much as 1 mg. was given daily. In laryngeal tuberculosis the effects were less marked, but with daily doses of from 0·05 to 0·1 mg. pain and hoarseness rapidly disappeared; infiltrative lesions of the vocal cords did best. Some beneficial effects were noted in tuberculosis of bones and of the urogenital tract, and in eye lesions the action was remarkable in 10 of 11 cases. Cepharanthin was also, it appears, used prophylactically in Japan in schools and factories. Striking results are described in the Kobura arsenal and in schools in Toyama, but full statistical information is not provided. Excellent results are claimed in all forms of leprosy and in whooping-cough.

[If these results are confirmed a new and interesting antibacterial substance will have been discovered.]

G. M. Findlay

3037. **The Clinical Value of Allergy to Tuberculin.** (Valeur clinique de l'allergie a la tuberculine)
I. BLUHM. *Poumon* [*Poumon*] **5**, 137–145, March–April, 1949. 19 refs.

The author reviews the literature concerning the development and maintenance of allergy in patients with tuberculous infection or having had inoculations of B.C.G., as shown by the tuberculin reaction. On re-testing 200 patients known to have had a positive tuberculin reaction from a few months to 5 years previously he found that only 2 had subsequently become negative. In these 2 cases he doubted whether, in fact, they had ever really been positive, one showing extensive reddening at the site of injection but no infiltration, and the other not having previously been tested in the same clinic. On the other hand, out of 400 cases giving a positive reaction after B.C.G. inoculation he found that 15·3% had subsequently become negative. He concludes that allergy produced by virulent tubercle bacilli is practically constant, but that produced by B.C.G. is not.

John Crofton

3038. **The Disease Pattern of Perforating Tuberculosis.** (Das Krankheitsbild der perforierenden Tuberkulose)
W. ISLER. *Schweizerische Zeitschrift für Tuberkulose* [*Schweiz. Z. Tuberk.*] **6**, 255–272, 1949. 4 figs., 17 refs.

A full account is given of 3 cases of atypical, malignant, perforating tuberculosis found amongst 102 necropsies on tuberculous patients at the Kantonsspital, St. Gallen. In contrast to " typical " perforations of caseous tracheobronchial lymph nodes into a bronchus, of intestinal ulcers into the peritoneal cavity, of cervical lymph-node abscesses, of caseous epididymitis through the scrotum, and of cold abscess from skeletal tuberculosis, " atypical " perforations such as those of a caseous pericarditis into the heart or of a lung cavity into the oesophagus are rare, multiple, and always fatal.

In the first case a primary pleural effusion in a young soldier developed into an open empyema, complicated by cavitation and mixed infection. Eventually a lung cavity perforated into the oesphagus and massive intestinal infection with multiple ulceration led to perforation and lethal peritonitis. In the second case an empyema resulted from perforation of a cavity into the interlobar

space; an abscess of the chest wall then led to open pyo-pneumothorax, with eventual perforation of another cavity into a bronchus, contralateral caseous pneumonia, and haematogenous miliary spread. In the third case, in a woman aged 62 with multiple cervical lymph-node abscesses and sinuses and perforation of bilateral apical empyemata into the supraclavicular fossae, a purulent caseous pericarditis perforated into the left auricle. Miliary spread resulted.

The 3 cases had in common complete failure of resistance from the start, leading to unusual multiple tissue breakdown with caseation and haematogenous spread. Sinus formation in a defenceless organism invites secondary infection which in turn aggravates the position by destroying the last reserves.

[The important lesson illustrated by these cases is that the one decisive factor in the course and prognosis of tuberculosis—as in other infections—is the host-parasite relationship, that is, the degree of immunity—innate and acquired—and the presence or absence of general resistance. This factor tends to be ignored by those who maintain that " the treatment of pulmonary tuberculosis is in fact the treatment of cavities ".]

E. G. W. Hoffstaedt

3039. **The Initial Stage of Post-primary Tuberculosis.** (Le stade initial de la tuberculose pulmonaire post-primaire)
E. HEDVALL. *Poumon* [*Poumon*] **5**, 75–84, March–April, 1949. 28 refs.

This paper summarizes previous literature, mainly German and Scandinavian, on the characteristics of post-primary tuberculous lesions in the lung. In conclusion the author gives his own views, based on serial radiographic studies after Mantoux conversion. He considers that post-primary lesions may present in one of two ways. In the " chronic " form, which is the commoner, the lesion is first detected about a year after Mantoux conversion, an attack of erythema nodosum, or the finding of a primary tuberculous lesion in the lung. The post-primary lesions consist of small foci usually 1 to 2 mm. in diameter, occasionally up to 5 mm., situated most commonly above the clavicle, sometimes high in the first intercostal space. The foci may be bilateral. They may heal, with or without treatment, leaving residual scarring or calcification or disappearing altogether. More often fresh shadows appear below the original foci, either shortly after the latter are first observed or, commonly, after the lapse of several years, during which the original foci may have remained static or tended to heal. These fresh shadows become confluent to form infiltrates, and the latter may then break down with subsequent bronchogenic spread. The initial foci are usually symptomless and the erythrocyte sedimentation rate is often normal, but tubercle bacilli may be obtained by guinea-pig inoculation or by culture of sputum or stomach washings.

The " acute " form of post-primary lesion develops directly from the pulmonary element of the primary complex or from foci in its immediate vicinity; the lesion is, therefore, frequently situated in the middle or lower zone of the lung. There is usually lymph-node enlargement, often followed by rapid progression to cavitation. Temperature and erythrocyte sedimentation rate are often raised and tubercle bacilli readily obtained from the sputum.

John Crofton

3040. **The Importance of Erythema Nodosum in the Prognosis of Primary Tuberculosis in the Adult.** (L'importance de l'érythème noueux dans le pronostic de la primo-infection tuberculeuse de l'adulte)
S. LÖFGREN. *Poumon* [*Poumon*] **5**, 147–156, March–April, 1949. 22 refs.

The author analyses 178 cases of erythema nodosum occurring in patients over the age of 15. Of these, 104 (58·4%) were of probable tuberculous origin—that is to say, there was a positive tuberculin reaction and radiographs of the lungs showed a primary tuberculous lesion. In 78 (43·8%) either tubercle bacilli were demonstrated or tuberculous complications supervened. He compares the incidence of pleural effusion (regarded as an unequivocal tuberculous infection), in those of his cases in which there were both erythema nodosum and a primary lesion, with that in series described by Heimbeck (*Zbl. ges. TuberkForsch.*, 1937, **45**, 537) and by Malmros and Hedvall (*Studien über die Entstehung und Entwicklung der Lungentuberkulose*, Leipzig, 1938) in nurses and medical students of a roughly similar age group. The results are expressed in the following table:

Authors	Type of Infection*	Sex	Number of Cases	Complicated by Sero-fibrinous Pleurisy
Heimbeck	E.N.	F.	43	5 (11·6%)
Heimbeck	Without E.N.	F.	241	20 (8·3%)
Löfgren ..	E.N.	F.	94	23 (24·5%)
Malmros and Hedvall	Without E.N.	F.	49?	1 (2·0%)
Löfgren ..	E.N.	F.+M.	103	25 (24·3%)
Malmros and Hedvall	Without E.N.	F.+M.	142	10 (7·0%)

*E.N. = erythema nodosum.

In each pair of series the difference in the number of cases of sero-fibrinous pleurisy within a year of infection is statistically significant, and the author concludes that erythema nodosum in primary tuberculous infection carries an unfavourable prognosis. Of 90 cases of erythema nodosum and a primary tuberculous infection β-haemolytic streptococci were isolated from the throat in 26, compared with 8 of 65 normal adults. In the former group 28 of 86 patients had antistreptolysin titres of over 200 units, compared with 11 out of 65 in the control group.

Finally, quoting figures previously published by himself (*Acta med. scand.*, 1946, **124**, Suppl. 174), the author relates the number of cases of primary tuberculosis in which tuberculous complications develop within a year to the height of the antistreptolysin titre.

He finds that tuberculous complications occurred within a year in 26% of cases with a low antistreptolysin titre (0 to 99), in 58% of cases with an average titre (100 to 199), and in 73% of cases with a high titre (200 and over).
John Crofton

3041. **Generalized Tuberculosis of Lymph Nodes.** (Uogólniona gruźlica węzłów chłonnych)
J. RYDYGIER and Z. RUSZCZEWSKI. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **4**, 353–356 and 388–390, March 21 and 28, 1949. 20 refs.

The problem of generalized tuberculosis of lymph nodes is discussed in the light of the authors' experience and of data collected from the literature.

The authors recognize different forms of the disease: exudative, granulating, productive with or without caseous degeneration, and productive with necrosis or blood clots. Combined forms were met with, but the exudative reaction dominated the picture. Clinically two main forms were recognized: acute and chronic. The acute may pass into the chronic stage and lesions undergo a process of calcification; the chronic condition is benign and often associated with intermittent exacerbations, but eventually ends in clinical recovery. This sequence of events may be interrupted, however, at any stage by secondary general spread which leads to death.

The progressive swelling of all lymph nodes, loss of weight, secondary anaemia, and changes in the morphology of the blood render difficult, in chronic cases, the differentiation from malignant granulomatosis, unless a biopsy specimen is studied. Sometimes the presence of multiple calcified nodes may aid recognition of the condition. A leucopenia of any considerable degree makes the prognosis more serious, except in extremely mild cases.
J. H. Czekalowski

3042. **Tuberculosis of the Breast.** (Contributo allo studio della tubercolosi della mammella)
G. IMPALLOMENI. *Archivio per le Scienze Mediche* [*Arch. Sci. med.*] **87**, 269–308, March, 1949. 7 figs., bibliography.

It was thought that the mammary gland was refractory to tuberculosis until the first description of the naked-eye appearance of the disease was given in 1829 by Astley Cooper. The author of this paper, originating from the Surgical Department of Turin City Hospital, reviews the literature of the subject and gives a description of 24 cases observed in Turin, of which 3 were in males. The incidence of tuberculosis of the breast amounted to 0·64% of all breast lesions diagnosed. The interval between appearance of the first symptoms and attendance of the patient at hospital ranged from 23 days to 36 months, and the patients' age from 23 to 75 years, the average being 36·4. In the literature, the lowest recorded age is 12 years. One-half of the author's patients were women who had borne children. In 5 cases there was a history of pleurisy on the same side, indicating the importance of the lymphatic connexions of the breast with the parietal pleura. In one case a tuberculous lesion was present in the fourth rib and in another in the lymph nodes. In no case was there any reason to believe that the infection was haematogenous or that it progressed along the milk-ducts. The patients complained of pain or discomfort in the affected organ, more marked in the premenstrual period, the hormonal changes of menstruation appearing to have an activating influence on the tuberculous infection of the breast. The general condition of the patients was good in 18 cases, moderate in 2, and poor in 4. There was only one bilateral case. The most frequent pathological forms were the fibrous and fibro-caseous forms with a single focus. The course of the disease was chronic and progressive. Diagnosis proved difficult in the 16 closed cases without fistula, of which only 3 were correctly diagnosed before operation; in 8 cases the diagnosis was carcinoma, in 4 benign tumour, and in one fibrocystic disease. The 8 cases with fistulae were all correctly diagnosed. The treatment was surgical, partial or total mastectomy being performed. There were no deaths in the author's series, the final result being satisfactory in all cases.
E. Forrai

3043. **Alcohol Injection of the Phrenic Nerve in Cavitation of the Lower Lobe** (Френикоалкоголизация при нижнедолевых кавернах)
D. L. BERKHMAN. Проблемы Туберкулеза [*Probl. Tuberk.*] No. 2, 10–15, March–April, 1949. 11 refs.

Alcohol injection of the phrenic nerve appears to be the favourite method of paralysing the diaphragm in the Soviet Union, and is employed with good effect in cases of tuberculous cavitation of the lower lobe. The author quotes the figures of several Soviet workers and adds 63 of his own cases. He prefers alcohol injection to phrenic avulsion because it produces the same effect and the process is reversible, while effects on the cardiovascular system are less severe. He holds that avulsion disturbs the autonomic nerve balance and may produce distressing palpitation and dyspnoea. Alcohol injection causes the three desired effects (rise in the cupola of the diaphragm, limitation of its excursions, and paradoxical movement) and little else, though in 2 of his cases Horner's syndrome was a temporary complication.

He divides his results into immediate (5 to 8 weeks after operation) and remote (6 to 18 months after operation), and classifies cases into four groups: " full effect ", " limited effect ", " no change ", and " deterioration ". By full effect he means a disappearance of the cavity and of tubercle bacilli from the sputum, and restoration of the patient's capacity for work.

Of his 63 cases, the first group of 7 were of unilateral disease with recent cavities on the basis of an exudative type of disease confined to one lower lobe; the second group of 19 were for the most part unilateral, but disease was not confined to the lower lobe; the third group of 3 were cases of primary tuberculosis; the fourth of 23 were cases of unilateral or bilateral disseminated disease; and the fifth included 11 cases of unilateral fibro-caseous disease.

In the whole series the immediate results were positive —that is to say, there was at least temporary benefit—in 36 (57·1%). The ultimate results were: full effect in all the 7 cases of the first group, and partial effect in 8 of the

19 cases of the second group and 1 case of the fifth. There was either no change or even deterioration in the remainder of the cases. From this he concludes that the method is unlikely to be effective in fibro-caseous disease and is definitely contraindicated in haematogenous disseminated tuberculosis. *L. Firman-Edwards*

3044. **Tuberculoma of the Lung Masquerading as Encysted Pleural Effusion**
N. WYNN-WILLIAMS. *British Journal of Tuberculosis* [*Brit. J. Tuberc.*] **43**, 6–11, Jan., 1949. 5 figs., 13 refs.

The author describes a tuberculoma in the upper lobe of the right lung in a woman of 41 years. The condition was first diagnosed as an interlobar effusion, until cavitation and the presence of acid-fast bacilli gave a clue to the real diagnosis. [The author gives a good account of the differential diagnosis of solitary round foci in the chest.] *J. L. Livingstone*

3045. **Relationship of the Pleural Fluid Sugar to Pulmonary Tuberculosis**
S. M. GELENGER and R. F. WIGGERS. *Diseases of the Chest* [*Dis. Chest*] **15**, 325–328, March, 1949. 1 ref.

The sugar content of the pleural fluid in 33 cases of exudative pleurisy accompanying a variety of conditions was estimated by the Folin–Wu method with a photo-electric colorimeter. In addition, the samples of fluid were cultured for tubercle bacilli and inoculated into 2 guinea-pigs; total cell count, total protein content, and specific gravity were also determined and stained smears examined. All cases were thoroughly investigated clinically and radiologically and the fullest use was made of laboratory investigations. By this means the aetiology was established in 31 of the 33 cases.

According to the sugar level the cases were divided into three groups. In group 1 were placed patients with a sugar level below 30 mg. per 100 ml. All 8 cases in this group were tuberculous. Group 2 consisted of 4 patients with a sugar level of 30 to 60 mg. per 100 ml.; 2 of these were tuberculous. In group 3 were 21 patients with a level above 60 mg., none of whom was tuberculous.

It is concluded that the finding of a low sugar level in a pleural effusion makes a diagnosis of tuberculosis most likely. In the presence of borderline values tuberculosis should be suspected until disproved by other means. A sugar level above 60 mg. per 100 ml. is unlikely to be associated with tuberculosis. *E. Nassau*

3046. **Pneumoperitoneum and Phrenic Paralysis in the Treatment of Pulmonary Tuberculosis. A Report on 188 Cases**
M. HANRAHAN. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] **6**, 112–124, March, 1949. 4 figs., 33 refs.

This paper is based on a study of all those patients treated for pulmonary tuberculosis by institution of a pneumoperitoneum at Crooksling Sanatorium and the Rialto Tuberculosis Hospital, Eire, during the period 1944–7. It is concerned mainly with the assessment of results, although the author also gives an account of his technique and a review of the complications of pneumoperitoneum treatment which is taken mainly from the literature.

The patients treated by phrenic paralysis reinforced by pneumoperitoneum totalled 131, the results, grouped according to the stage at which the treatment was instituted, being as follows: (1) After failure to induce a pneumothorax. In this group the disease became quiescent in only 6 cases out of 43. (2) After abandonment of an unsatisfactory pneumothorax. In this group the disease became quiescent in 12 cases out of 38. (3) In conjunction with an inadequate pneumothorax. In this group the disease became quiescent in 5 cases out of 10. (4) In cases unsuitable for any other form of treatment. Here the disease in most cases was far advanced and in 3 cases only out of 40 was it subsequently regarded as quiescent. The author also analyses the effect of phrenic paralysis and pneumoperitoneum in relation to cavity site. Out of 89 patients in whom the cavity was situated above the hilum a satisfactory result was obtained in 20, and of 6 patients with a cavity below the hilum the result was satisfactory in 4. (In this analysis no far-advanced cases are included.) Pneumoperitoneum was used alone in 57 cases, in only one of which was the disease considered to have become quiescent.

The main conclusions reached are: (1) Pneumoperitoneum alone is of little value. (2) Pneumoperitoneum with phrenic paralysis is of little value in cases where the pleural surfaces are widely adherent and in advanced cases. (3) Pneumoperitoneum with phrenic paralysis is of most value (*a*) when the cavitation is below the hilum, and (*b*) when a partial pneumothorax is being maintained at the same time or when the pleura is relatively free after a pneumothorax has been abandoned.

[This is a sound and useful paper. However, the conditions required for the recognition of quiescence are stated rather vaguely and, in the section concerned with the situation of cavities, it is not quite clear what constitutes a " satisfactory " result.] *Howard Nicholson*

3047. **Closure of Tuberculous Pulmonary Cavities, As Accomplished by Residence in the Immobilizing Lung Chamber**
A. L. BARACH, C. EASTLAKE, J. H. CULLEN, and G. F. HERBEN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **139**, 833–836, March 26, 1949. 4 figs., 13 refs.

In this paper the authors describe a method whereby lung rest may be achieved by means of an immobilizing chamber as an alternative to the usual methods employed in the treatment of cavitary pulmonary tuberculosis. It is claimed that by use of this apparatus adequate pulmonary ventilation is provided, with constant lung volume and without discernible motion of the chest and diaphragm, and that more complete rest both for the lungs and for the laryngo-tracheo-bronchial tree is thus achieved than by any other method hitherto used. A period of 10 hours' treatment daily for 4 to 5 months has resulted in marked improvement in a number of cases which had previously resisted treatment.

The immobilizing lung chamber, in which the patient is totally enclosed, provides a means of equalizing the air pressure on both sides of the chest wall and diaphragm while ventilation of the lungs is taking place. Alternating positive and negative pressures, 55 to 65 mm. of mercury above and below atmospheric pressure, are produced within the chamber 20 to 25 times a minute, this being sufficient to ventilate the lungs of the patient. Resistance in the respiratory passages during the initial stage of each phase is simultaneously counter-balanced by means of a partition around the neck of the patient which enables a slightly different pressure to be exerted, as necessary, on the chest and abdominal wall, from that in the chamber as a whole. The resulting immobility after the patient has learnt to renounce voluntary respiration is illustrated by radiographs with lead markers on the chest wall, the outline of which remains sharp after an exposure of 10 minutes.

The degree of physical and mental rest achieved in the absence of voluntary respiration is striking. Pulse rate, systolic blood pressure, and temperature are diminished. The patients co-operate well and their morale is good. The first series of 11 patients with advanced bilateral pulmonary tuberculosis treated by this method and described in 1941 (Barach, *Amer. Rev. Tuberc.*, 1941, **42**, 56) have been followed up; of the 6 patients in whom clinical arrest was obtained 2 were lost sight of one year after discharge, one had to return to bed on 3 occasions for 4 months over a period of 11 years, but was well most of that time, one was well for 4 years when a fall caused a relapse, and 2 patients who had advanced cavities at the time of treatment have been well and working for 5 and 6 years respectively. Among the failures 2 patients required more than one course of chamber treatment and received inhalations of " promin " before cavity closure was obtained. In a more recent series of 11 patients the cavity closed and the sputum became negative after a single course in 9, of whom 6 had previously been unsuccessfully treated with pneumothorax.

In the authors' opinion, the use of the chamber in early cases of cavity and exudative lesions is justifiable and, combined with chemotherapy, may be of value in otherwise hopeless cases with low immunological resistance. The cause of cavity closure is discussed and a number of questions are posed concerning the wider use of the chamber, to which further experience alone will provide the answers. *Ronald S. McNeill*

3048. **Tuberculostatic Effect of Furacin *in vitro* and *in vivo***

E. Wolinsky, V. Wetzel, and W. Steenken. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 483–487, March, 1949. 2 figs., 8 refs.

Furacin (5-nitro-2-furaldehyde semicarbazone), which was known to have antibacterial activity *in vitro* and *in vivo* against various organisms, was tested against *Mycobacterium tuberculosis*, H37 Rv strain. Complete inhibition was produced at a concentration of 1 in 20,000 in four different fluid media, including the Dubos " tween "-albumin medium, when the inoculum was 0·03 mg. dry weight of bacilli per 5 ml. of medium. The drug was bactericidal at 1 in 5,000 concentration. Furacin-resistant strains could not be obtained by repeated exposure of H37 Rv to graded concentrations of the drug in Dubos medium, but the combination of the drug with streptomycin in this medium did not prevent, though it delayed, the development of streptomycin-resistance in this strain. When guinea-pigs were infected with H37 Rv, furacin, in its maximum tolerated dose of 35 mg. per kg. daily for 2 months (suspended in 10% gum acacia and given by mouth with a syringe), did not affect the course of the disease. *P. D'Arcy Hart*

3049. ***para*-Aminosalicylic Acid in the Treatment of Various Forms of Tuberculosis of the Lungs and Pleura.** (L'acido *para*minosalicilico nella cura delle varie forme di tubercolosi pleuro-polmonare)

A. Scarpa and R. Rizzi. *Riforma Medica* [*Rif. med.*] **63**, 369–374, April 23, 1949. 11 figs., 24 refs.

Pulmonary and pleural tuberculosis was treated in 24 cases with daily doses of 9 to 21 g. (according to age) of *p*-aminosalicylic acid (PAS) by mouth for periods of 45 to 120 days, and the drug was also given by intrapleural and intracavitary instillation and by aerosol. In " a high proportion " of cases there was an appreciable improvement in the general condition of the patient, with gain in weight, fall in temperature and erythrocyte sedimentation rate, improvement in the blood picture and vital capacity, and decrease in the quantity of sputum. Improvement in the radiological appearances, however, was much less notable. No severe degree of intolerance to the drug occurred and there was no evidence of toxicity.

The authors have the general impression that PAS exerts a favourable though limited effect on certain forms of tuberculosis, in particular empyema, recent exudative disease, bronchial lesions, and cavities under Monaldi drainage, and especially where PAS can be brought into direct contact with the lesion. The effect is definitely less than that of streptomycin, but the drug might well be used in conjunction with the antibiotic to deal with streptomycin-resistant strains of tubercle bacillus.

E. G. Sita-Lumsden

3050. **First Results of Treatment of Tuberculous Empyema with *p*-Aminosalicylic Acid.** (Primi risultati della terapia degli empiemi tubercolari con acido *p*-aminosalicilico)

F. Ingrao, N. Belli, M. Morellini, and C. Cattaneo. *Lotta contro la Tubercolosi* [*Lotta c. Tuberc.*] **19**, 61–81, Jan., 1949. 3 figs., 8 refs.

Doses of 0·5 to 2 g. of *p*-aminosalicylic acid were injected intrapleurally twice daily in 5 cases of tuberculous empyema. The total aggregate dose per case varied between 17·5 and 121 g. The period of administration ranged from 20 to 59 days. At 3 to 5 months from the end of treatment, 3 of the patients remained free from pleural exudate. In one case, exudate persisted in a serous form. One of the patients died from pulmonary tuberculosis after the empyema had healed.

J. Cauchi

3051. **Antagonism Between Effects of *p*-Aminosalicylic Acid and Salicylic Acid on Growth of *M. tuberculosis***
G. IVÁNOVICS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 462–463, March, 1949. 10 refs.

The author, using the Dubos liquid medium, with inoculum of 0·0001 mg. dry weight per 5 ml. of the medium, studied the effect of combinations of sodium salicylate and the sodium salt of *p*-aminosalicylic acid (NaPAS) on growth of several strains of tubercle bacilli, judged turbidimetrically. With NaPAS at or near its minimal completely inhibitory concentration (when used alone), the presence of salicylate at 4 to 12 times the molar strength of the NaPAS resulted in partial [but not full] growth of one of the strains—that is to say, partial antagonism of the inhibition by NaPAS was produced. [It should be noted that at this concentration salicylate alone would produce some degree of inhibition.] The tuberculostatic effect of NaPAS was not antagonized by a number of compounds related to salicylic acid—that is, the effect appeared to be specific to the latter. The concentrations of salicylate required to antagonize NaPAS were larger than those of *p*-aminobenzoic acid (PAB), 1 mol. of which could antagonize 4 ml. of NaPAS. PAB did not antagonize the inhibitory effect of sodium salicylate (when the latter was at completely inhibitory concentration), nor did pantothenic acid.

P. D'Arcy Hart

3052. **Intermittent Dosage Schedules of Streptomycin with Resultant Prolonged Sensitivity of *M. tuberculosis***
V. F. DEYKE, M. W. FISHER, L. A. JAMES, and L. J. SIDES. *Annals of Internal Medicine* [*Ann. intern. Med.*] **30**, 619–634, March, 1949. 20 refs.

The authors review the problem of streptomycin therapy, and in particular that of bacterial resistance to drugs. Results of experimental work by Feldman, and later by Corper and Cohn, indicated that streptomycin might exert a " threshold of remote sustained action ". Intermittent streptomycin administration had given a favourable therapeutic response in guinea-pigs, and the authors initiated an investigation in an attempt to substantiate these findings in human beings.

Sixteen patients with pulmonary tuberculosis were selected; in all, sputum was positive, as demonstrated by direct smear examination or culture, before streptomycin was given; 8 had advanced cavitation. All were observed for at least a month before the initiation of streptomycin treatment. The drug was given intramuscularly, 2 g. in 5 divided doses, every 3rd day in 8 cases, every 4th day in one case, and every 5th day in 7 cases. The treatment period was 120 days in 11 cases, 90 days in 2 cases, and 65 to 69 days in 3 cases. Full clinical evaluations were made at monthly intervals, with a concluding analysis in the post-treatment period.

The clinical response was considered excellent in 7 cases, moderate in 6. Excellent radiological response is reported in 8 cases, moderate in 4. Sputum conversion occurred during treatment in 8 cases. In the opinion of the authors, the clinical and radiological results were comparable with those obtained previously with 1 and 2 g. of streptomycin daily. [This is a statement of a general impression; no data are submitted for comparison.] No patient had subjective signs of streptomycin toxicity. Of the 8 patients with a positive sputum, the tubercle bacilli remained sensitive in 7. This important finding is confirmed by further results given in an addendum: of 31 cases given 1 g. daily and remaining positive after 70 days' treatment, 23 showed drug resistance, compared with 4 of 28 cases receiving the drug intermittently.

The authors discuss the advantages of schemes of streptomycin dosage which aim at avoiding emergence of drug-resistant strains. *M. Daniels*

3053. **A Clinical Report of Three Cases of Vitamin B Deficiency Occurring During Streptomycin Therapy**
J. SUMNER. *Tubercle* [*Tubercle*] **30**, 62–65, March, 1949. 6 refs.

While receiving 1 g. daily of streptomycin, given intramuscularly, 3 patients with pulmonary tuberculosis out of 154 so treated showed signs of vitamin-B deficiency. They developed angular stomatitis, sore tongue, and widespread dermatitis. They improved when given riboflavin or nicotinic acid, and relapsed when these were withheld. Culture of their faeces yielded a greatly reduced growth of *Bacterium coli*, which were sensitive to streptomycin, 1 unit per ml. of medium; one month after the end of streptomycin treatment numerous *Bact. coli* were present in each case. It is suggested that streptomycin produced avitaminosis by reducing the number of intestinal organisms responsible for the synthesis of vitamin-B substances. *L. M. Franklin*

3054. **Resistance of the Tubercle Bacillus to Streptomycin**
B. BLATTBERG and H. EHRHORN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **34**, 358–365, March, 1949. 24 refs.

Thirty-nine patients from whom tubercle bacilli had been isolated received 1 g. streptomycin intramuscularly every day for 90 to 180 days. Sputum from these patients was cultured at intervals on Petragnani slopes after concentration by Petroff's method. Any tubercle bacilli isolated were transferred to a modified Dubos liquid medium. Streptomycin-sensitivity tests were carried out by the serial dilution method in the same medium, the inoculum being 0·1 ml. of a 6 to 10-day culture, and results were read after 14 days' incubation. The highest concentration of streptomycin permitting growth of bacilli in specimens obtained before treatment was 1 μg. per ml. Strains observed after treatment were regarded as resistant if growth occurred in 10 μg. per ml. or more. After 30 days' treatment no resistant strains were detected but thereafter an increasing number of strains was found to be resistant—2 out of 15 isolated on the 60th day, 6 of 17 isolated on the 90th day, 11 of 25 isolated between the 100th and 120th days, and 9 of 19 isolated on the 120th day. Many of the resistant strains were able to grow in concentrations of 1,000 μg.

streptomycin per ml. and it is interesting to note that in 4 patients the degree of resistance increased after the cessation of treatment. (This phenomenon had also been found in 2 patients previously treated with a different dose schedule.) Tubercle bacilli disappeared from smears and concentrates of sputum in 41% of the 39 patients treated, but in only 3 patients (8%) did cultures become negative for 3 successive months.

The authors summarize the findings of a number of other workers on streptomycin-resistant strains of tubercle bacilli, and discuss their results in relation to treatment schedules. *Mary Barber*

3055. **Results of Streptomycin Treatment of Tuberculous Meningitis in the Adult after 2 Years' Experience.** (Résultats du traitement de la méningite tuberculeuse de l'adulte par la streptomycine après deux années d'expérience)
E. Bernard, B. Kreis, A. Lotte, P. Chiche, and P. Y. Paley. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **65**, 526–530, 1949. 4 figs.

3056. **Antibacterial Activity of D-Usnic Acid and Related Compounds on *M. tuberculosis***
A. Marshak, W. B. Schaefer, and S. Rajagopalan. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **70**, 565–568, April, 1949. 6 refs.

See also Sections Pharmacology and Therapeutics, Abstracts 2711, 2720; Radiology, Abstract 2762; and Pathology, Abstract 2778.

LEPROSY

3057. **Two-and-a-half Years' Experimental Work on the Sulphone Group of Drugs**
R. G. Cochrane, K. Ramanujam, H. Paul, and D. Russell. *Leprosy Review* [*Leprosy Rev.*] **20**, 4–64, Jan.–April, 1949. 16 figs., 14 refs.

The records are given of 54 cases of leprosy (all lepromatous), mainly in Indian adult males, treated with sulphones at the Lady Willingdon Leprosy Sanatorium, Madras, S. India. The results are tabulated and compared with the results obtained with hydnocarpus at the same hospital between 1938 and 1947. The drugs used were "diasone" (orally), "sulphetrone" (orally and parenterally), and diaminodiphenyl sulphone ("promin") (parenterally), the effective dosage being some 10 to 20 times higher with oral than with parenteral administration. With all these drugs, uniform clinical improvement was obtained, diaminodiphenyl sulphone having the most rapid effect, diasone the least. Among the less advanced cases (bacteriological index 2) negative smears were found in from 16 to 26 months with sulphones, a result very similar to that with hydnocarpus injections (20 to 24 months). The sulphones, however, led to a higher percentage of negative smears and had the advantage that the painful intradermal injections of hypnocarpus were avoided. Diasone was the least toxic, causing occasional nausea, vomiting, and haematuria. Sulphetrone in some cases caused anaemia (cured by iron), severe occipital headaches, and cyanosis. Diaminodiphenyl sulphone occasionally caused jaundice and peripheral neuritis in addition to the above. Later experiences with injections of this drug appear promising, but until more is known about its toxicity the authors recommend treatment with sulphetrone, injections of 7 ml. of 50% aqueous solution being given twice weekly.
Clement Chesterman

3058. **Effect of "Promin" (Diaminodiphenylsulphone) on Ocular Complications of Leprosy.** (Ação das diaminodifenilsulfonas sobre as complicaçoes oculares da lepra)
A. U. Zavalia. *Revista Brasileira de Leprologia* [*Rev. brasil. Leprol.*] **17**, 5–17, March, 1949. 3 figs.

To 25 lepers, 20 of whom had ocular complications, intravenous injections of "promin" were given 6 days a week to a total of 100 injections. After a rest of 30 days a second course was given, and so on for periods between 7 and 20 months. The amount injected daily was 12·5 ml. (or 5 g. of the substance).

In the 5 controls no ocular lesions appeared. The remainder of the patients were divided into three groups. In the first group of 7 patients lesions were limited to the cornea; in 3 the condition improved, in 2 there was no change, and in 2 the process spread to the anterior segment of the uvea. These changes bore no relation to the effect of the drug on the general condition. In the second group of 5 patients with more severe corneal involvement and a nodular or miliary iritis, only one patient responded, the lesions becoming stationary. In the remainder the condition became worse in that the iritis became more severe; in 2 cases transient exacerbations of acute iridocyclitis were observed. In the third group of 8 patients with severe corneal infiltrates, nodular or miliary iritis, and a diffuse iridocyclitis, only one patient responded to treatment. The condition in the remainder became progressively worse, although in some cases skin and mucosal lesions simultaneously improved. *S. S. B. Gilder*

3059. **Intradermal Administration of Promin**
G. Herrera. *International Journal of Leprosy* [*Int. J. Leprosy*] **16**, 439–442, Oct.–Dec., 1948.

The author describes the effect of "promin" (promanide) 40% solution when injected directly into aural and nasal lepromatous lesions which had proved resistant to intravenous administration of the drug. The solution was introduced slowly into the centre of the nodule, preferably from behind in the case of the ear. The size of individual injections varied and was only exceptionally greater than 0·5 ml. and the daily total given by all routes did not exceed 12·5 ml. Local injections were repeated, when necessary, every 7 to 8 days. Care was taken to prevent the solution from coming into contact with the skin and healthy tissues.

The treated nodules softened and occasionally disappeared without discharging. More frequently the centre of the nodules became fluid, and the nodules were then destroyed by expulsion of the contents by manual

pressure, the overlying skin either rupturing spontaneously or else being pierced by a wide-calibre needle. The resultant scars usually became unnoticeable.

Out of a total of 30 patients, in 20 the disappearance of nodules was complete within 80 days; in the remaining 10 there was improvement. Intradermal injection of promin did not greatly affect macules or plaques.

W. H. Horner Andrews

3060. **The Blood Picture in Leprosy**

S. KIANG and G. H. CHOA. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **217**, 269–276, March, 1949. 13 refs.

The blood of 36 lepers from Western China was examined. Many forms of treatment for leprosy had been tried and some of the patients also suffered from ascaris or hookworm infestation. Moderate hypochromic anaemia was almost constant, and in 7 patients it was macrocytic. Anisocytosis, poikilocytosis, punctate basophilia, and polychromasia were not found. Reticulocyte counts were low, mostly about 0·2%. Erythrocyte sedimentation rates were raised in all except 4 cases, and the Kahn test was positive in all except 2. Moderate polymorphonuclear leucocytosis was prominent in the lepromatous cases. Eosinophilia occurred in a third of the cases, and the eosinophil count did not fall after the expulsion of intestinal worms. In contrast to the experience of other observers monocytosis was found to be of no value in prognosis. *E. Neumark*

3061. **Diffuse Lepra**

M. E. OBERMAYER, S. C. BONAR, and R. ROSENQUIST. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **12**, 243–248, April, 1949. 3 figs., 6 refs.

Diffuse lepra was first described by Lucio in 1851 under the name of " spotted " or " lazarine " lepra. It was again identified in 1937 by Latapí and his co-workers, who believe it to be an exclusively Mexican disease, while even in Mexico the distribution is regional, most cases occurring in the state of Sinaloa where 60 to 70% of lepromatous cases are of the diffuse type.

The two special features of the condition are: diffuse infiltration of the skin of the whole body, and a peculiar reaction known as " Lucio's phenomenon " or erythema necroticans. The first signs of disease are often anidrosis, numbness of the hands and feet, and slowly progressive loss of eyelashes and eyebrows. Nodules are not formed, but the skin is diffusely infiltrated and, although normal in appearance, gives an abnormal reaction to histamine. *Mycobacterium leprae* can usually be obtained by the scraped incision method from any region of the skin. In some cases there is chronic diffuse swelling of the face, hands, and legs and there are often widespread small telangiectases, particularly on the face and trunk.

The characteristic lepra reactions appear after 3 or 4 years, being few at first and more numerous later. The lesions are irregularly shaped, tender, painful, erythematous, slightly infiltrated macules, 0·5 to 1 cm. in diameter. They appear first on the legs and to a lesser extent on the arms, involving the face and trunk much later. The development and involution of individual macules are uniform and rapid, the cycle occupying 2 weeks. The lesions darken and become purpuric in 3 to 4 days, central necrosis develops, and an eschar forms and falls off in a few days leaving a superficial, sharply circumscribed, atrophic scar. At times there is deeper ulceration with consequent delay in healing and the production of a residual scar. Lesions in all stages of development may be seen at the same time. Many of the manifestations commonly encountered in ordinary lepromatous lepra are seen in the diffuse type; but it is noteworthy that ocular involvement and the formation of cutaneous nodules have not been observed. The Wassermann and Kahn tests are always positive and the erythrocyte sedimentation rate is extraordinarily high. The reaction to the conventional lepromin (Mitsuda) test is negative. Untreated, the disease terminates fatally in about 8 years, with progressive weakness, loss of weight, and anaemia, but the use of sulphones has improved the prognosis. A case in an American of Mexican descent is described.

James Marshall

SCARLET FEVER

3062. **The Course of Scarlet Fever in Children in the Post-war Period.** (Течение скарлатины у детей в послевоенный период)

O. A. CHUMAERSKAYA. Педиатрия [*Pediatriya*] No. **2**, 16–18, March–April, 1949.

The author summarizes the findings in 1,214 cases of scarlet fever seen in a Moscow children's clinic between June, 1945 and July, 1947. The proportion occurring in the youngest age group [limits not stated] was 5·7% in 1945, 23·8% in 1946, and 28% in 1947. The number of cases of toxic, septic, and other severe forms of the disease fell from 6·2% of the total in 1945 to 2·9% in 1947. In 1945 4 patients died, but there were no deaths in 1946 or 1947. The decrease in the number of severe cases and deaths is attributed by the author to two factors: (1) reduced virulence in later epidemics; and (2) an increase in the use in treatment of such measures as sulphonamides, penicillin, and blood transfusion. But there has also been a general improvement in the standard of nutrition of the children seen. In 1944 38·8% were well-nourished, 48·5% under-nourished, 2·5% very under-nourished, and 0·2% in a state of exhaustion; in 1945 55·6% were well-nourished, 43·5% under-nourished, and 2·7% very under-nourished; and the corresponding figures for 1947 were 63%, 30·9%, and 2·2%. [The criteria of nourishment are not stated.] The incidence of acute nephritis fell from 4·5% of cases in 1945 to 1·5% in 1946, while no case of acute diffuse glomerulonephritis occurring in the first 10 days of the disease was seen in 1947, only 4 cases of non-albuminuric oedema occurring after the 10th day being seen.

[This paper, although short, is especially interesting in view of the paucity of recent Soviet health statistics. It would be of interest to know how far some of the facts given correspond to changes in the composition of the population of Moscow during the transition from war to

peace-time conditions. The phrase in the original which has been translated as " under-nourished " implies a lowered standard of nutrition; the exact implications of the lowered standard are not clear, and the use of the word " under-nourished " is based on the context.]

Jeffrey Boss

3063. **The Character of Monocytic Reaction in Scarlet Fever.** (Характер моноцитарной реакции при скарлатине)

A. L. STRUTSOVSKAYA. Педиатрия [*Pediatriya*] No. **2**, 4–12, March–April, 1949. 3 figs.

The author classifies the mononuclear leucocytes as promonocytes, monocytes, or polymorphomonocytes. On this basis she has carried out 364 differential monocyte counts on the blood of 32 children suffering from scarlet fever. She takes as the normal count for children between 7 and 12: promonocytes, 18 to 20%; monocytes, 34 to 40%; and polymorphomonocytes, 42 to 47%.

In scarlet fever of all types and degrees of severity there is a marked relative increase in the number of polymorphomonocytes, though this shift is most marked in the first 5 days and in the more severe cases. It gradually diminishes, but is generally still evident on the 30th day of the disease. The tables of monocyte counts given indicate that the increase is statistically highly significant, even in the sixth 5-day period of the disease. The author assumes the polymorphomonocytes to be the oldest, and interprets her findings as evidence of a marked depression of monocyte production at the beginning of the disease.

[It would be helpful to know the author's cytological definition of a monocyte, and of the three forms distinguished. Monocyte-like cells arise experimentally very easily by metaplasia, and the precise significance of changes in monocyte counts is not known. The consistency of the findings, however, in the hands of one worker using one set of criteria, makes the results of great interest. The absolute monocyte counts in these cases would have been interesting.] *Jeffrey Boss*

3064. **Haemoglobin Exchange in Scarlet Fever.** (О гемоглобиновом обмене при скарлатине)

T. V. FOKINA. Педиатрия [*Pediatriya*] No. **2**, 18–22, March–April, 1949. 4 figs.

This work is based on observations made in a series of 37 cases of scarlet fever in children, in 8 of whom complications developed. In the acute stage of the disease and during the time complications were present the blood haemoglobin level was reduced by 15 to 20% of its original value. With increasing anaemia there was a greater output of stercobilin, a five-fold increase being found in some cases. Regeneration of erythrocytes, as indicated by a rise in the reticulocyte count, nearly always took place after the pyrexial period; this regeneration, however, did not always match the great breakdown of haemoglobin that had occurred in the acute phase of the disease. The degree of anaemia was generally proportional to the excretion of stercobilin. In mild cases there might be no anaemia. The author concludes that not only iron, but also plenty of protein and substances rich in pyrrole rings, should be given after the anaemia has set in.

[In the present state of our knowledge of the mechanism of the formation of haemoglobin, it is not easy to assess the value of the author's advice about non-iron-containing haemoglobin constituents. There would seem to be a field here particularly suited to investigation by isotopic tracers.] *Jeffrey Boss*

PROTOZOAL INFECTIONS

3065. **Mel B in the Treatment of Human Trypanosomiasis**

E. A. H. FRIEDHEIM. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **29**, 173–180, March, 1949. 5 refs.

In a previous paper (*Ann. trop. Med. Parasit.*, 1948, **42**, 357) the author reported the cure of early and advanced sleeping sickness (*Trypanosoma gambiense*) with " melarsen oxide " (*p*-melaminylphenylarsenoxide or *para*-(1 : 2-diamino-1 : 3 : 5-triazinyl-6)phenylarsenoxide, a tervalent derivative of " melarsen " or sodium *p*-melaminylphenyl arsonate or " acide triazinarsinique "). The apparently cured patients were under observation for periods up to 10 months.

In the present paper the author records results obtained with " mel B ", an alkyl mercapto derivative of melarsen oxide containing tervalent arsenic, which was given daily by intravenous injection of a 5% solution in propylene glycol, 3 to 14 injections of 2 to 4 mg. per kg. body weight being given in 50 advanced cases of Gambian sleeping sickness in French West Africa. Trypanosomes disappeared rapidly from the blood, lymph nodes, and cerebrospinal fluid; in 20 patients the number of leucocytes and amount of protein in the cerebrospinal fluid returned to normal, in 22 the protein level alone remained above normal, in 1 the reverse occurred, and in 7 the figures for both cells and protein remained above normal. The observation periods ranged from 12 to 222 days. No toxic effects of the drug were recorded.

The author recommends the following routine for mass treatment of all stages of sleeping sickness: " Two series of 4 intravenous doses of 3·6 mg. per kg. each, applied one dose a day for 4 consecutive days, the two series being separated by a rest period of one week." In very severe cases the injections of the first series should be given at 3 to 4 days' interval to avoid reactions of the Herxheimer type. *J. F. Corson*

3066. **The Active Form of Tryparsamide, TPB, in the Treatment of Human Trypanosomiasis**

E. A. H. FRIEDHEIM. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **29**, 181–184, March, 1949. 7 refs.

Tryparsamide is rapidly excreted and its trypanocidal action is produced by the very small percentage of the dose which is reduced in the body from the quinquevalent to the tervalent form of arsenic. Hitherto preparations of reduced tryparsamide have been too unstable and toxic

for use in sleeping sickness, but the author has prepared a stable and detoxified form, named " TPB ", which is a white powder containing 21·6% of tervalent arsenic. In collaboration with the Sleeping Sickness Service of French West Africa, the drug was tried in 10 cases of sleeping sickness with infection of the central nervous system—the so-called second stage. The first 5 patients received a single intravenous dose of 1·5 mg. per kg. body weight [the text gives 1·5 gr.—a mistake], and no trypanosomes were found in the lymph nodes or blood from 1 to 24 hours later, nor during the next 3 days. The other 5 patients were given the drug by mouth, usually in daily doses of 7 to 25 mg. per kg. body weight for 7 to 14 doses; trypanosomes disappeared from the lymph nodes within 24 hours and the cell count and protein content of the cerebrospinal fluid were normal when determined 7 to 162 days later.

TPB had no effect on tryparsamide-resistant strains of *Trypanosoma gambiense* in the cerebrospinal fluid of one patient with sleeping sickness, and only temporarily cleared the trypanosomes from the blood of an infected guinea-pig. The drug may be of value, however, in regions free from tryparsamide-resistant trypanosomes.

J. F. Corson

3067. **Treatment of Kala-azar with Pentamidine Isethionate. A Study of 55 Cases.**
A. N. HAZARIKA. *Indian Medical Gazette* [*Indian med. Gaz.*] **84**, 140–145, April, 1949. 5 refs.

The author treated 55 cases of Indian kala-azar with pentamidine isethionate; of these, 34 were resistant to antimony. The maximum single dose varied from 0·75 to 2 mg. per lb. (454 g.) of body weight, and the number of injections in a course ranged from 10 to 20. The drug was given either intravenously or intramuscularly, intravenous administration being associated with mild toxic symptoms. Oedema developed in 4 patients and was attributed to toxic action of the drug. Three patients died and one defaulted, giving a cure rate of 94·44%, which is comparable to that achieved with " neostibosan ". The relapse rate in 42 cases followed up was 38·09% and was similar in patients resistant to antimony and those non-resistant. It is suggested that higher dosage and intravenous administration may reduce the relapse rate. The late neurological sequelae of stilbamidine treatment were not encountered.

J. L. Markson

3068. **Toxoplasmosis.** (Toksoplazmoza)
M. WILK-WILCZYŃSKA. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **4**, 364–367 and 395–396, March 21 and 28, 1949. 4 figs., 16 refs.

An interesting case of congenital toxoplasmosis in a girl 3 years of age is reported. The child was mentally backward and could only utter inarticulate sounds. The skull was asymmetrical and slight hydrocephalus was present. The fact that the left eyeball was much smaller than the right was noticed by the mother a few days after the child was born. There was complete blindness of the left eye; in the right there was a sharply defined area of atrophy of the retina and choroid, oval in shape, in the macular region. Radiographs revealed multiple calcified lesions like peppercorns or rice grains in the brain, but these were confined to the middle fossa. Apart from nystagmus, excessive salivation, and signs of hydrocephalus no neurological signs were present. The cerebrospinal fluid was normal; serological tests were not conclusive but the clinical syndrome alone justified the diagnosis of congenital toxoplasmosis. This is the first case of toxoplasmosis reported in Poland, but the author believes that the condition is more common than is generally recognized.

J. T. Leyberg

MALARIA

3069. **Southwest Pacific Vivax Malaria. Clinical Features and Observations Concerning Duration of Clinical Activity**
E. HILL and D. S. AMATUZIO. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **29**, 203–214, March, 1949. 3 figs., 37 refs.

From July, 1945 to March, 1948 inclusive, the author made a clinical study of 328 cases of South-west Pacific vivax malaria in young ex-service men at the Veterans Hospital, Minneapolis. The features studied were the symptoms, duration, relapse rate, and response to treatment and these are analysed from a statistical point of view. Prodromal symptoms other than fever and malaise occurred in 46%, splenomegaly in 37·6%, and hepatomegaly in 15·1%; the relapse rate after treatment with chloroquine was 56%, with mepacrine 60%, relapses occurring much earlier after chloroquine. The relapse rate decreased with further attacks but the proportion of relapses in each group remained about the same. In one group 24·5% were cured in the first year, 52·9% in the second year, and 18·3% in the third year. The findings are set out in tables and figures, and reference is made to the results of other observers.

J. F. Corson

3070 (*a*). **Some Observations on the Action of Quinine, Atebrin, and Plasmoquine on *Plasmodium vivax***
M. J. MACKERRAS and Q. N. ERCOLE. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **42**, 443–454, March, 1949. 7 figs., 16 refs.

3070 (*b*). **Observations on the Action of Quinine, Atebrin and Plasmoquine on the Gametocytes of *Plasmodium falciparum***
M. J. MACKERRAS and Q. N. ERCOLE. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **42**, 455–463, March, 1949. 2 figs., 8 refs.

As members of the entomological team of the L.H.Q. Medical Research Unit at Cairns, Queensland [see Fairley, *Trans. R. Soc. trop. Med. Hyg.*, 1945, **38**, 311], during the recent world war the authors investigated the action of certain drugs on strains of *Plasmodium vivax* and *P. falciparum* obtained in the New Guinea area. White volunteers were infected by *Anopheles punctulatus*

punctulatus, bred mosquitoes were infected from them, and the effects of the drugs on the development of the parasites in both man and the mosquito were studied. Detailed observations on a few selected cases are given, and morphological changes in *P. vivax* are shown on coloured plates.

1. *Plasmodium vivax*.—Quinine sulphate, 10 gr. (0·65 g.) thrice daily, caused degeneration and retarded the growth of the developing forms, and no true schizonts were seen after the first dose; mature gametocytes were little affected and mosquitoes were infected on each day of treatment, but the authors consider that the growth of young gametocytes was inhibited. In daily doses of 5 or 10 gr. (0·32 to 0·65 g.) quinine usually failed to suppress sporozoite-induced infections and the parasites remained infective to mosquitoes. Atebrin (mepacrine) dihydrochloride, 1 g. on the first day and 0·4 g. daily for 6 days, acted like quinine; in none of the volunteers receiving regular suppressive doses were parasites found in the blood, but in one man, with both trophozoites and gametocytes, doses of 0·05 g. on alternate days reduced the number of trophozoites but had no effect on the gametocytes. Plasmoquine (pamaquin), 30 mg. of base daily for 5 days, was given to 2 patients infected by injections of blood and suffering from quotidian fever, and a single dose of 10 mg. was given to another patient with numerous gametocytes in his blood. Degeneration of all stages of trophozoites resulted, but after the dose of 10 mg. mosquitoes could be infected up to 30 hours later but not at 42 hours. Some parasites of a single brood of *P. vivax* were more susceptible than others to quinine, and trophozoites of all ages were less susceptible to quinine than to mepacrine. Both drugs seem to act by inhibiting metabolism of haemoglobin, whereas pamaquin is a more general protoplasmic poison.

2. *Gametocytes of P. falciparum*.—Quinine sulphate, 5 to 10 gr. daily, had a very deleterious effect on young gametocytes or their precursors; no parasites were present in the blood of most volunteers receiving these doses, and when parasites were found they were usually few in number. Mepacrine, even in therapeutic doses, had little or no effect on gametocytes, except that a varying proportion of them had no pigment or very little; these were infective to mosquitoes and developed into unpigmented oocysts. Pamaquin had a pronounced action on the gametocytes, a dose of 10 mg. making them non-infective to mosquitoes within 15 hours and causing them to disappear from the blood in 3 or 4 days.

J. F. Corson

3071. **Acquired Resistance to Proguanil (Paludrine) in *Plasmodium vivax***

D. R. Seaton and E. M. Lourie. *Lancet* [*Lancet*] **1**, 394–395, March 5, 1949. 4 refs.

A strain of *Plasmodium vivax* was maintained by inoculation of blood into two series of patients; in one series subinoculations were always made before treatment with proguanil was given, but in the other series subinoculations were made from one patient to another after the former had received repeated small doses of proguanil, in order to see whether the parasites would become resistant to the drug. In the former series of patients fever and parasitaemia ceased within 48 hours after three daily doses of 1·25 mg. of proguanil. In the latter series the strain had had 28 passages after 20 months; slight resistance to the drug was noticed at the 5th passage and increased so that between the 20th and 24th passages (after 14 to 18 months) 10 mg. daily for 3 days had no effect on the fever or the parasites, and the lowest dose needed to clear the blood of parasites and stop the fever was about 50 mg. daily for 3 days. At the 27th and 28th passages (after 20 months) 100 mg. daily for 3 days had no effect on the fever or parasites but the strain was susceptible to 300 mg.; resistance to proguanil had therefore increased more than eighty-fold. At the 23rd passage the resistant strain was transmitted by *Anopheles stephensi* to a patient and was found to be still fully resistant to 10 mg. daily for 3 days; higher doses could not be tried.

The authors give several reasons for concluding that ordinary clinical use of proguanil in prophylaxis and treatment will not cause *P. vivax* to become resistant to the drug. [See also these *Abstracts*, 1948, **3**, 222 and 223; Rollo *et al.*, *Ann. trop. Med. Parasit.*, 1948, **42**, 241; Hawking and Perry, *Lancet*, 1948, **2**, 850].

J. F. Corson

3072. **Some Pharmacological Actions of Paludrine**

J. R. Vane. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **4**, 14–21, March, 1949. 6 figs., 31 refs.

Paludrine (proguanil) has a delayed toxic action in mice, an effect decreased by the simultaneous injection of neostigmine. The toxicity therefore might have been due to the inhibition of cholinesterase, but paludrine was found by the author to antagonize the action of acetylcholine or of vagal stimulation in experiments on frogs, guinea-pigs, rabbits, and cats. Like other compounds which antagonize acetylcholine, paludrine lengthened the refractory period of rabbit auricular tissue. Other antimalarial drugs—quinine, mepacrine, and pamaquin—have a similar effect. Paludrine, like quinine, had a curare-like action on nerve-muscle preparations from the cat and rat, and like mepacrine, pamaquin, and quinine caused vasodilatation in the perfused vessels in the hind leg of the dog and of the cat. The dilatation was partially abolished by antihistaminic agents, suggesting that paludrine may release histamine from the tissues.

R. Wien

3073. **Antimalarial Compounds as Antagonists of Adenosine**

J. Madinaveita and J. Raventós. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **4**, 81–92, March, 1949. 4 figs., 26 refs.

A study of the antagonism of the action of adenosine by antimalarial drugs was undertaken with the object of obtaining information on the mode of action of this type of drug. The techniques employed were (1) study of the effect of adenosine on the isolated hen's caecum before and after addition of antimalarials, and (2) measurement of the duration of the auriculo-ventricular block produced

in the guinea-pig heart by the intravenous administration of adenosine, the antimalarials being given either intravenously or by mouth. The first method proved to be unsatisfactory since, although it was possible to demonstrate an antagonism between antimalarials and adenosine, the intense relaxation of the caecum produced by the antimalarials themselves made the assessment of the antagonism somewhat difficult. The second method was therefore adopted and three types of experiment were performed: (*a*) acute, in which the antimalarial compounds were administered by slow intravenous injection and electrocardiographic records were taken; (*b*) "chronic" in which the guinea-pigs received by mouth two doses daily of the compound, being tested for 3½ days before the experiment was performed; and (*c*) experiments on heart-lung preparations of guinea-pigs, the electrocardiograph leads being placed in the superior vena cava and on the apex of the heart.

Mepacrine, quinine, pamaquin, chloroquine, proguanil and a number of other compounds were employed. A correlation was observed between antimalarial activity and degree of inhibition of the action of adenosine, and it was inferred that the antimalarial activity of these compounds is in some way related to their ability to interfere with the biological processes in which adenosine is concerned. Mepacrine was found to have the greatest antagonism in the "chronic" experiments. Proguanil was a strong antagonist in the "chronic" experiments but a weak antagonist in the "acute" experiments; the difference being explained by the assumption that in the "chronic" experiments a metabolite with antagonistic properties was formed during the period of administration. Unlike the other antimalarials examined, proguanil did not antagonize the action of adenosine in heart-lung preparations, although the blood of proguanil-treated guinea-pigs did antagonize this action. This gave support to the view that proguanil is metabolized in the body to more actively antimalarial constituents.

R. Wien

3074. **Infection of Mammalian Erythrocytes by the Avian Malaria Parasite, *Plasmodium lophurae***

R. B. McGhee. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **71**, 92–93, May, 1949. 1 fig., 4 refs.

In an attempt to secure the infection of mammalian cells in chick embryos infected with *Plasmodium lophurae* the best results were obtained with erythrocytes of Swiss mice. Injection of 0·2 ml. of twice-washed erythrocytes was made intravenously into White Leghorn embryos of 10 days' incubation 2 days after infection of the embryos by *P. lophurae*. The mouse cells maintained their morphology and were readily parasitized, infection occurring as early as 12 hours after introduction. The parasites developed normally in the mouse cells, producing merozoites after 36 hours. The results of these experiments suggest a closer relationship between avian and mammalian parasites than previously suspected, and that resistance to infection may lie in the serum constituents rather than in the erythrocytes.

J. L. Markson

3075. **Report on Malaria in Borneo. An Account of the Work of the Malaria Research Department, North Borneo, 1939–42.**

J. MacArthur. Malaria Research Department, Labuan, North Borneo. 1949, 250 pages.

This report, just completed in the interior of North Borneo at the time of the Japanese occupation, has had a difficult and hazardous career. The manuscript was twice confiscated by the Japanese, was blown up by an allied bomb, and eventually rescued after 11 months from a waterlogged crater. It gives an exhaustive account of malaria and malarial vectors in North Borneo and should be read in its entirety by those interested.

G. M. Findlay

3076. **Hemoglobinuria (Blackwater Fever) in Monkeys: A Consideration of the Disease in Man**

R. H. Rigdon. *American Journal of Pathology* [*Amer. J. Path.*] **25**, 195–209, March, 1949. 7 figs., 35 refs.

Twenty-seven rhesus monkeys received intraperitoneal, subcutaneous, and intravenous injections of blood containing *Plasmodium knowlesi*. Ten of these animals developed haemoglobinuria. The author deals with clinical and renal pathological studies of these ten monkeys. When haemoglobinuria was present at the time of death the glomeruli showed few significant changes. The epithelial cells of the convoluted tubules were always injured, sometimes swollen sufficiently to occlude the lumen, sometimes fragmented, and sometimes desquamated into the lumen. The cytoplasm contained small masses of yellowish-brown pigment, some staining faintly with Prussian blue. There were large amounts of similar pigments in the lumina of the tubules, especially the collecting tubules. The epithelium of Henle's loop was desquamated, particularly in the vicinity of large casts. Casts varied considerably from animal to animal and from nephron to nephron. Sometimes they were large, homogeneous, and pale pink on staining. In some tubules they were composed of groups of granules staining deeply with eosin, approximately equal in size to an erythrocyte but sometimes considerably smaller. Other tubules contained desquamated epithelial cells and also amorphous and yellowish-brown material. Casts were present in large numbers in the collecting tubules, but in some animals were also numerous in the convoluted tubules. There was no significant change in the interstitial tissue. The small blood vessels were filled with parasitized cells; there were no specific vascular lesions. In one monkey, which was killed shortly after recovery from haemoglobinuria, the kidneys were normal in size and colour, and no casts were present.

According to the author, the younger monkeys with severe infections were especially prone to develop haemoglobinuria, the appearance of which was influenced by the severity of the infection. The carbon-dioxide combining power was found to be low in one animal, suggesting a severe terminal "acidosis". The presence or absence of either oliguria or anuria was not determined in these experiments. The author nevertheless discusses

the incidence of these phenomena in monkeys and in blackwater fever in man. He states, " the quantity of material within the lumina in the renal tubules in these monkeys appears to be insufficient to produce anuria in the manner suggested for cases of so-called 'lower nephron nephrosis'. Certainly, casts in the lumina of tubules may produce anuria; however, anoxia and shock appear to contribute more to the occurrence in monkeys with haemoglobinuria accompanying malaria ". He points out that in severe malaria symptoms of shock may occur and, as glomerular filtration is determined by blood pressure, it is significantly decreased in the presence of shock. He suggests that such a mechanism is " more significant in producing anuria in blackwater fever than obstruction in the lumina of the tubules ".

[The significance of anoxia in the pathogenesis of malarial lesions was clearly defined by the author in 1942. His views coincide closely with recent English and French opinion, but for some reason or other much of the relevant literature is not discussed in the present paper.] *B. G. Maegraith*

OTHER INFECTIOUS DISEASES

3077. **Spectacular Improvement Produced by Heparin in a Case of Acute Articular Rheumatism.** (Amélioration spectaculaire d'un cas de rhumatisme articulaire aigu par l'héparine)
E. DONZELOT, H. KAUFMANN, E. CHARTRAIN, and J. NORY. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **65**, 475–478, 1949. 1 fig.

A woman of 25 years, suffering from mitral disease, suddenly developed intense general joint pains with pyrexia (38° to 39° C.; 100·4° to 102·2° F.). After 2 months' illness, the disease was treated by giving heparin (150 mg. in 24 hours) intravenously for 3 days; the dose was doubled on the 4th and 5th days, and on the 5th day the pyrexia ended by crisis, the temperature subsequently being normal. With the end of the pyrexia the pains ceased and did not recur. On the 3rd to 8th days (that is, until 3 days after the end of the pyrexia) 0·75 g. of " 3277 RP " (" phenergan ") was given in each 24 hours. For 6 days after the end of pyrexia, 5 million units of penicillin were given daily. Before this treatment the disease had proved resistant to both sodium salicylate (12 g. a day orally or 3 g. orally with 2 g. intravenously) and penicillin.

The paper was read only 9 days after the crisis of the disease and it is not therefore known how permanent this cure may be. [The erythrocyte sedimentation rate is not mentioned.] *Jeffrey Boss*

3078. **Liver Function during Infectious Mononucleosis**
J. W. BROWN, J. LER. SIMS, E. WHITE, and J. E. CLIFFORD. *American Journal of Medicine* [*Amer. J. Med.*] **6**, 321–328, March, 1949. 44 refs.

This report is based on an analysis of 83 cases of infectious mononucleosis observed in the department of student health of the University of Wisconsin. Most patients were subjected to two or more tests of liver function at various stages of the disease. The results of one or more tests were considered abnormal in 75 of the patients. Cephalin–cholesterol flocculation was abnormal in 85% of the cases tested, bromsulphalein retention was abnormal in 49%, and icterus index in 38%. Liver function tended to return to normal within 2 to 6 weeks, and there was no suggestion that liver damage severe enough to cause insufficiency in later life ever occurred. *P. C. Reynell*

3079 (*a*). **Studies on *Listeria monocytogenes*. I. Isolation of a Monocytosis-producing Agent (MPA)**
N. F. STANLEY. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **27**, 123–131, March, 1949. 3 figs., 28 refs.

3079 (*b*). **Studies on *Listeria monocytogenes*. II. Role of Listeria in Infectious Mononucleosis**
N. F. STANLEY. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **27**, 133–142, March, 1949. 26 refs.

A lipid was extracted from the disrupted bacterial cells of a strain of *Listeria monocytogenes* recently isolated from an infected person. When inoculated intravenously into rabbits this lipid caused a monocytosis; it was non-antigenic. In rabbits, lethal infections by *L. monocytogenes* are characterized by multiple necrosis of the liver and spleen; injection into rabbits of saline extracts of the necrotic liver produced monocytosis. In this animal the liver is probably the site of greatest multiplication of the organism and thus of the formation of the substance causing monocytosis.

The second paper records the results of an investigation into the possible aetiological role of *L. monocytogenes* in glandular fever. Of 20 cases of this disease, in 35% there were both a positive Paul–Bunnell reaction and a significantly high titre of agglutinins to *L. monocytogenes*. In 65% of the cases the sera did not agglutinate the organism, although 35% gave a positive Paul–Bunnell reaction. In one case a rise in titre, as demonstrated by both the Paul–Bunnell and the agglutination tests, occurred during the illness. The stimulation of antibodies to *L. monocytogenes* appeared to be specific, because agglutinins to other bacteria, such as those of the typhoid group, did not develop. Blood cultures for *L. monocytogenes* were consistently negative, but it is noted that even in experimental non-fatal infections of rabbits it is usually impossible to recover the organism from the blood.

It is suggested that glandular fever may be caused by more than one infective agent and that a proportion of cases may be due to *L. monocytogenes*. It is, however, impossible to explain the positive Paul–Bunnell reaction in such cases. The lipid fraction causing monocytosis, and the polysaccharide and protein fractions of the organism, did not themselves agglutinate sheep erythrocytes or stimulate the formation of sheep-erythrocyte agglutinins in rabbits. It was not possible to reduce the Paul–Bunnell titre of sera by adsorption with suspensions of *L. monocytogenes*. *D. G. ff. Edward*

See also Section Respiratory Disorders, Abstract 2882.

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S. S. B. GILDER, B.Sc., M.B., B.S.

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